The Practical Veterinarian

Veterinary Epidemiology

Margaret R. Slater

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NOTICE

Veterinary epidemiology is an ever-changing field. Standard safety precautions must be followed, but as new research and clinical experience broaden our knowledge, changes in treatment and drug therapy may become necessary or appropriate. Readers are advised to check the most current product information provided by the manufacturer of each drug to be administered to verify the recommended dose, the method and duration of administration, and contraindications. It is the responsibility of the licensed prescriber, relying on experience and knowledge of the patient, to determine dosages and the best treatment for each individual patient. Neither the publisher nor the editor assumes any liability for any injury and/or damage to persons or property arising from this publication.

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Series Preface

The Practical Veterinarian series was developed to help veterinary students, veterinarians, and veterinary technicians find answers to common questions quickly. Unlike large textbooks, which are filled with detailed information and meant to serve as reference books, all the books in The Practical Veterinarian series are designed to cut to the heart of the subject matter. Not meant to replace the reference texts, the guides in our series complement the larger books by serving as an introduction to each topic for those learning the subject matter for the first time or as a quick review for those who already have mastered the basics of each subject.

The titles for the books in our series are selected to provide information for the most common subjects one would encounter in veterinary school and veterinary practice. The authors are experienced and established clinicians who can present the subject matter in an easy-to-understand format. This helps both the first-time student of the subject and the seasoned practitioner to assess information often difficult to comprehend.

It is our hope that the books in The Practical Veterinarian series will meet the needs of readers and

serve as a constant source of practical and important information. We welcome comments and suggestions that will help us improve future editions of the books in the series.

Shawn P. Messionnier, D.V.M.

Preface

This book had its genesis in my teaching epidemiology and public health to first-, third-, and fourth-year veterinary students. In trying to make the material as relevant to clinical practice as possible, my courses were revised over the years. Eventually, I began to use evidence-based medicine (now evidence-based care [EBC] or practice) as an approach that merged the clinical perspective with epidemiology. In human medicine, EBC has swept into the profession with the development of courses, books, and databases specifically designed to help practitioners get the best information for their practices. In veterinary medicine, EBC is slowly creeping in: It appears in some conferences, articles, and book chapters. In working through the examples for class (and this book), it became clear that the quality and quantity of material available to the practitioner of veterinary medicine have not yet caught up with that available to the practitioner of human medicine. It is hoped that this book will serve to bring EBC to the attention of a larger veterinary audience, summarize what is known and applicable to veterinary medicine, and help veterinarians with their patient care and client education.

I am especially appreciative of my contributors, Norma Funkhouser and Laura Robinson. Ms. Funkhouser's

years of experience as a medical librarian and dealing with veterinary students, graduate veterinarians, and faculty provide her with invaluable background when it comes to finding information on all things veterinary. Dr. Robinson has had extensive first-hand experience in dealing with zoonoses and outbreaks in the real world. Her position in Zoonosis Control provides interaction with veterinarians in all types of practices and settings in the context of these topics.

I would also like to thank my epidemiologic colleagues from around the world (you know who you are!) who have encouraged and supported my efforts in veterinary epidemiology. In particular, Drs. Janet Scarlett and Hollis Erb were instrumental in getting me hooked on epidemiology as a profession.

M.R.S.

Introduction

This book is meant to be a reference for the application of epidemiology in the veterinary practice setting. It is designed to be used by veterinary students and practitioners, as well as interns and residents in teaching programs. The principles of epidemiology are set into a clinical context. This approach allows the veterinarian or student to use them to help keep up with and apply the ever-increasing body of knowledge to provide the best available care in veterinary practice for the individual patient or a herd, shelter, or flock of patients.

What is epidemiology? Most simply, it is the study of diseases and health in populations. Diseases include not only the classic infectious diseases and disease outbreaks but also chronic diseases like arthritis, cancer, and renal failure. Also included are injuries and exposures to environmental contaminants. Factors that maintain good health and quality of life are also within the purview of epidemiology. In this context, questions about the causes of animals being relinquished to animal shelters or about animal well-being in long-term kennel settings may also be addressed by epidemiologists. Populations are considered to be any pertinent group, such as all dogs seen in a veterinary practice, horses at a stable, dairy cattle in New York state. And although many small

animal clinicians are most accustomed to diagnosing and treating individual animals, information about groups of animals similar to their patients is needed in order to keep up to date on new information and keep clients as informed as possible.

How can epidemiology best help a busy practitioner with patients and clients? One approach is called evidence-based care (EBC). It is a method of using epidemiology to directly improve clinical practice. This approach consists of four parts: (1) converting the health care issue into an answerable, searchable clinical question; (2) finding the best available evidence to address the clinical question; (3) appraising that evidence for its quality and for its applicability to the current situation; and (4) incorporating the best evidence into clinical practice. Evidence-based care supplements clinical judgment; it never replaces it. The physical examination and history provide vital and irreplaceable information on treatment, diagnosis, prognosis, and causation. Epidemiology also has a central role in helping veterinarians deal with disease outbreaks and preventive health care. In order to provide the practitioner with all of the necessary background in epidemiology, this book has been divided into four parts: (1) incorporating evidence-based care in the clinical setting; (2) zoonotic diseases; (3) outbreaks and promotion of health in populations; and (4) simple biostatistics. The first major section begins with developing the clinical

question from an issue or lack of information arising in practice and finding the evidence from printed and electronic sources as well as experts. Next, an overview of the types of studies and information commonly obtained is provided. This overview includes the key points to determine the quality of the results for different types of clinical questions. There are four types of common clinical questions: (1) treatment and prevention; (2) diagnosis and testing; (3) prognosis, and (4) causation or etiology. The second major section of the book includes chapters on zoonotic diseases of clinical importance by species and organ system. A discussion of to whom and how to report these diseases is presented, with tips on finding locally pertinent information. Outbreaks and the promotion of health are topics of the third major section and are addressed at the level of the group or population. Approaches to investigating outbreaks and to developing disease prevention programs are outlined. Finally, a brief review of simple statistical concepts and analyses is given using an intuitive nonmathematical approach because statistics have become a crucial part in understanding and evaluating the validity of many studies and articles.

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Why Evidence-Based Care?

Underlying the evidence-based care (EBC) approach is the understanding that there is a hierarchy of the quality of evidence available. Some types of studies, all other things being equal, provide better quality information than others. The randomized controlled clinical trial and reviews of this study type provide the best evidence. Observational studies (in which the investigator records natural exposures or does not control the assignment of treatments) provide the next level of quality. Studies that use intermediate events rather than clinically

relevant endpoints or make clinical predictions based on physiologic effects are third in the hierarchy. And clinical impressions, anecdotes, and observations provide the weakest forms of evidence.

A second underlying principle of EBC is the crucial importance of the client's values, situation, and relationship to the patient. This principle is played out in the decision-making process for the veterinarian and client in terms of cost, previous experiences, time commitments, convenience, family concerns, long-term goals, and risk-benefit ratios. This decision process goes on constantly in practice but may not be explicitly considered as an important client issue. This may be particularly true in a primary care setting, where the most commonly selected choice may be substituted for providing a broader range of choices to the client due to time constraints. In addition, the opportunity for referral may not be offered based on preconceived notions of what the client is interested in doing for the patient.

Clinical questions are the motivators behind incorporating evidence into patient care. These questions are the result of an unknown or unfamiliar problem in the context of dealing with patients and clients. For example, in treating a dog with unilateral primary glaucoma, the value of treating the currently normal eye might be an issue. Does prophylactic treatment delay or even prevent glaucoma in the unaffected eye of a

dog with primary glaucoma? This is a clinical question (the answer is usually yes). A clinical question is composed of who (the patient's general signalment), what (the problem of interest), the action (what intervention or test), the comparison (if needed) and the outcome (what endpoint is in question). By starting with a specific question, the uncertainty in the clinical situation will be clarified. However, in finding the information, a more general approach to the search may be needed, depending on the source material. See Chapter 3 for some examples and pitfalls in searching the veterinary literature.

Clearly, time constraints, availability of evidence (both actually published and access to publications), and lack of training in accessing and interpreting the evidence can be substantial barriers to using EBC in the practice setting. EBC does not need to be used for all patients. Many routine types of patient care can be handled on *autopilot* because decisions about how best to handle the situation have already been determined by previous experience and knowledge. Sometimes, a phone call or e-mail message to a colleague or teacher will provide the necessary information. But in some circumstances, the same question has been asked by multiple clients or the same debate about the advisability of a specific treatment or product occurs and the correct answer is not clear. Perhaps, there are new products on the market that are

unfamiliar, or new research published or perhaps the veterinary profession still really does not have the answer. The application of EBC is the solution to determine whether or not this new information or products should be incorporated into the practitioner's repertoire of care.

In its most formal application, EBC also requires that the practitioner assess how well EBC is being incorporated into the practice of veterinary medicine. In veterinary practice, there are no data that specifically evaluate the barriers and facilitators of EBC. In fact, continuing education in general (which would include EBC) is often required by employers or state licensing boards, but the subject has rarely been evaluated for its impact on or incorporation into practice. Studies on adult learning would tend to indicate that passively listening to a lecture is a very poor method of learning new information or techniques. In 1996, an article was published that measured the effect of a hands-on certification course in dairy production medicine on the farm management and herd performances.[1] The authors found that there was a dramatic effect on important herd production parameters. This finding has implications for the importance of incorporating key information and skills into practice on an ongoing basis, as well as the need for evaluation of the effectiveness of all forms of continuing education, including EBC.

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Polzin DJ, Lund E, Walter P, Klausner J. From journal to patient: Evidence-based medicine. In Bonagura JD (ed): *Kirk's Current Veterinary Therapy XIII*. Philadelphia: W.B. Saunders Company, 2000:2–8.

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Sources of Epidemiologic Information

Norma Funkhouser

In today's technology-driven world, access to current, accurate information is vital. Information resources in veterinary epidemiology are difficult to identify because of their multidisciplinary nature. This chapter attempts to identify some specific information resources in veterinary epidemiology categorized by format, both print and electronic. Talking with other people is often the fastest way to obtain the most current information, especially on research projects.

Printed Format Information

Print resources can be separated into monographs (books), journals, specific journal articles, conference proceedings, and other ephemeral or *grey* literature, including pamphlets and brochures.

Monographs

Monographs are books on a single major topic. The following list includes some of the most recent monograph publications in the field of veterinary epidemiology:

- Toma B, Vaillancourt J-P (eds). *Dictionary of Veterinary Epidemiology*. Ames, Iowa: Iowa State University Press, 1999, ISBN 081382639X, 284 pages, paperback, approx. $60.00. Defines epidemiologic terms and terms from several related fields, including ecology, statistics, economics, pathology, and preventive medicine. Examples are given of term usage and many cross-references. No index.
- Toma B. *Applied Veterinary Epidemiology and the Control of Disease in Animal Populations*. France: Maisons-Alfort, 1999, ISBN 9290444878, 536 pages, approx. 360 FRF ($46 USD). Translated by Alexandra Shaw from the original French publication in 1996.
- Jongejan F, Camus E, Goff WL (eds). *Tropical Veterinary Medicine: Molecular Epidemiology, Hemoparasites and Their Vectors, and General Topics*. New York: New

York Academy of Sciences, 1998, ISBN 1573311421, 550 pages, paperback. A report on sessions held at a May 1997 conference in Montpelier, France.

- Thrusfield M. *Veterinary Epidemiology* (ed 2). Oxford: Blackwell Science, 1995. ISBN 0632048514, 496 pages, approx. $57.00.
- Martin SW, Meek AH, Willeberg P. *Veterinary Epidemiology: Principles and Methods*. Ames, Iowa: Iowa State University Press, 1987, ISBN 0813818567, 356 pages.
- Smith R. *Veterinary Clinical Epidemiology: A Problem-Oriented Approach* (ed 2). Boca Raton, FL: CRC Press, 1995, ISBN 0849324459, 279 pages, approx. $85.00.This book focuses on the application of epidemiologic principles and techniques to problems regularly faced by veterinary practitioners. Numerous examples from the veterinary literature indicate how experience with patients can be used to explore issues of importance in the practice of veterinary medicine while controlling for bias, confounding, and chance. The first part of the book focuses on the application of epidemiology in medical decision making. The second part focuses on the epidemiology of disease in populations and outbreak investigation. A glossary of epidemiologic terms and an extensive bibliography are also included. The second edition includes myriad updates to reflect the expanding use of epidemiologic

methodology in clinical research. This book serves as both a teaching resource for veterinary epidemiology and a reference on the application of epidemiologic methods in veterinary clinical research. Review posted to *http://amazon.com*.

Other veterinary epidemiology publications focusing on a specific disease condition or microorganism include the following:

- Tidholm A. *Canine Idiopathic Dilated Cardiomyopathy: Epidemiology, Histopathology and Pathophysiology,* Swedish University of Agricultural Sciences, Uppsala, Sweden, 2000, ISBN 915765932X, various paging, dissertation.
- Saeed AM, Gast RK, Potter ME (eds). Salmonella Enterica Serovar Enteritidis *in Humans and Animals: Epidemiology, Pathogenesis, and Control.* Ames, Iowa: Iowa State University Press, 1999, ISBN 0813827078, 443 pages, approx. $160.00. A comprehensive review of an emerging pathogen with responses by public health authorities on controlling outbreaks of the disease.
- Finley D. *Mad Dogs: The New Rabies Plague* (Louise Lindsey Merrick Natural Environment Series, No 26). College Station: Texas A&M University Press, 1998, ISBN 0890968225, 232 pages, paperback, approx. $15.00. A chronicle of a rabies outbreak on the Texas border, including political and side issues inhibiting institution of an effective U.S. rabies vaccination program.

Journals

The most widely used journal in this field is *Preventive Veterinary Medicine*, published by Elsevier Science, New York. This is the official journal of the International Society of Veterinary Epidemiology and Economics (ISVEE). The web site for subscriptions and further information is http://www.elsevier.nl/locate/prevetmed/. This journal is also available in full-text electronic format to libraries and individuals subscribing to the print edition.

Other journals, which may occasionally publish veterinary epidemiology articles in the subject area of general epidemiology, are as follows, in alphabetical order by journal title:

- *American Journal of Epidemiology*, Williams & Wilkins, Baltimore, MD.
- *Epidemiological Bulletin*, Pan American Health Organization, Washington, D.C.
- *Epidemiology and Infection*, Cambridge, University Press, New York, NY.
- *Epimonitor*, Roger Bernier Publishers, Roswell, GA.
- *European Journal of Public Health*, Almqvist & Wiksell International, Stockholm, Sweden.
- *Genetic Epidemiology*, Alan R. Liss, New York.
- *International Journal of Epidemiology*, Oxford University Press, London.
- *Journal of Clinical Epidemiology*, Pergamon Press, New York.

- *Journal of Epidemiology and Biostatistics*, ISIS Medical Media, Oxford.
- *Journal of Epidemiology and Community Health*, British Medical Association, London.
- *Neuroepidemiology*, S. Karger, New York.

JOURNAL ARTICLES Journal articles on veterinary epidemiology are widely published. Some of the major peer-reviewed journals in this subject area were listed earlier.

All of the relevant journals listed in the previous section (except *Epimonitor*) are indexed in the MEDLINE bibliographic database, published by the National Library of Medicine in Bethesda, Maryland. Searching that database for bibliographies of journal articles is available to the public worldwide at no charge for anyone with access to the Internet/World Wide Web. The database posted on the web is called PubMed and is found at the URL http://www.ncbi.nlm.nih.gov/pubmed/. Searches can also be done on request to a medical or veterinary library.

Additional journal articles may be located by searching the CAB International bibliographic database, CAB Abstracts. CABI indexes veterinary and agricultural journals worldwide and makes available a much larger collection of journal articles than Medline. However, access is restricted to those who subscribe to their services. Information on pricing is available at

http://www.cabi.org/. Searches of this database may also be requested from any veterinary library. A listing of all North American veterinary school libraries, their hours of operation, phone and fax numbers, and contact person's name is published as part of the membership directory of the American Veterinary Medical Association.

The Royal College of Veterinary Surgeons has also posted a bibliography of *Evidence-based Veterinary Medicine* journal articles on its web site at http://www.rcvs.org.uk/. These articles cover a 10-year span of time from 1988 to 1998.

Links to tables of contents of over 150 veterinary journals are posted on the web by Jean-Paul Jette, veterinary librarian at the University of Montreal, as each journal is received in that library. This web site also has lists titles of proceedings that have been published. The URL is *http://www.medvet.umontreal.ca/biblio/vetjr.html.*

Photocopies of articles located can be requested from any veterinary library or through the interlibrary loan department of a local public library.

Conference Proceedings

Conference proceedings of professional groups in the area of veterinary epidemiology are published irregularly. Many groups meet every year; some less frequently. A list of two of the most pertinent includes

- Salman MD, Morley PS, Ruch-Gallie R. *ISVEE 9: Breckenridge, Colorado, August 6–11, 2000: Proceedings: 9th Symposium of the International Society for Veterinary Epidemiology and Economics*, 2000, 1415 pages. http://www.cvmbs.colostate.edu/cveadss/isvee/isvee.htm. This symposium occurs every 3 years.
- Goodall EA, Thrusfield M. *Society for Veterinary Epidemiology and Preventive Medicine: Proceedings of a Meeting Held at the University of Edinburgh on the 29th, 30th, and 31st of March 2000*. ISBN 09480734446, 243 pages. http://www.vie.gla.ac.uk/svepm/proceedings.html. This conference is annual.

"Grey" Literature

"Grey" literature consists of written material that has not been published by the usual publishing companies but is still printed and available to purchase (or download). The National Animal Health Monitoring System (NAHMS) results from USDA are one example of grey literature. APHIS pamphlets are another. More examples are provided in the following list:

- Animal and Plant Health Inspection Service. *Highlights of Layers '99 Study Results:* Salmonella enterica *serotype Enteritidis*, USDA APHIS, 2000, 2 pages.Animal and Plant Health Inspection Service. *Fumonisin B1 in Horse Grain/Concentrate on U.S. Horse Operations*, USDA APHIS, 2000, 2 pages.

- Animal and Plant Health Inspection Service. *Internal Parasites & U.S. Horses*, USDA APHIS, 2000, 2 pages.

The preceding U.S. government publications are available from the USDA and indexed in major bibliographic databases, making their existence a bit easier to verify. Many authoritative, informative veterinary publications, such as studies done by pet food or animal pharmaceutical companies, are published irregularly and not indexed anywhere. Obtaining copies is most difficult. A nearby College of Veterinary Medicine library can be contacted for additional resources. A listing of North American veterinary libraries can be found in the Membership Directory of the American Veterinary Medical Association, giving the address of the library, the hours of operations, services provided, and the name of a contact person.

General Epidemiology

General epidemiology works with an emphasis on human medicine abound. For purposes of this book, the following is a list of some of the monograph publications with a more clinical emphasis:

- Gordis L. *Epidemiology* (ed 2). Philadelphia: W.B. Saunders, 2000, ISBN 072168338, 320 pages, $36.95. Includes sections on the epidemiologic approach to disease, using epidemiology to identify

the cause of disease and applying epidemiology to evaluation and policy. Concludes with a chapter on ethical and professional issues in epidemiology.

- Greenberg RS, Boring JR, Eley JW. *Medical Epidemiology* (ed 3). New York: Lange Medical Books/McGraw-Hill, 2001. ISBN 0838562957, 215 pages, $34.95. Includes a basic introduction to epidemiology and chapters on clinical trials, cohort studies, case-control studies and interpretation of the epidemiologic literature.
- Katz DL. *Clinical Epidemiology and Evidence-Based Medicine: Fundamental Principles of Clinical Reasoning and Research.* Thousand Oaks: Sage Publication, 2001, ISBN 0761919384, 280 pages, paperback, $32.95.
- Hulley SB, Cummings SR, Browner WS. *Designing Clinical Research: An Epidemiologic Approach* (ed 2). Philadelphia: Lippincott Williams & Wilkins, 2001. ISBN 0781722187, 336 pages, paperback, approx. $40.00. Emphasizes common sense approach to planning and implementing clinical research. Good information on designing research projects, study design, data collection, quality assurance, and grant proposal writing.
- Szklo M, Javier Nieto F. *Epidemiology: Beyond the Basics*. Gaithersburg, MD: Aspen Press, 2000, ISBN 0834206188, 495 pages, approx. $55.00. An intermediate text comparing different study designs, epidemiologic methods, and bias.

The following lists a couple of practical "handbook" (lots of outlines and basic principles) general epidemiology books:

- Torrence ME. *Understanding Epidemiology* (Mosby's Biomedical Science Series). St. Louis: Mosby, Inc. 1997, ISBN 0815188870, 180 pages, paperback, approx. $28.00.
- Streiner DL, Norman JR. *PDQ Epidemiology* (ed 2). St. Louis: Mosby, Inc. 1996, ISBN 0815190468, 160 pages, paperback, approx. $20.00.

Electronic Resources

As of 2001, there are very few electronic monograph publications in epidemiology. Certainly, as publishers make decisions on licensing, additional resources will become available in electronic format. A few that are available are presented in the following list:

- http://www.bmj.com/epidem/epid.html. Epidemiology for the Uninitiated, 4th edition by D. Coggen, Geoffrey Rose and DJP Barker, BMJ Publishing Group, 1997.
- http://www.fjc.gov/EVIDENCE/science/sc_ev_sec.html. The *Reference Manual on Scientific Evidence* found at the above URL on the internet is published by the U.S. Federal Judicial Center. It contains background information on scientific evidence based on statistical and epidemiological analyses for use by

U.S. federal judges. There is a section titled *Reference Guide on Epidemiology*.

Full-Text Electronic Journal Articles

More and more veterinary journals are being made available on the internet in full-text electronic format. A few are free to the user. Usually, a journal publisher's web page permits access to the table of contents to recent or archived issues and encourages the user to subscribe to the journal to get access to the electronic format. Some titles are only available in electronic format, but most still market the printed copy with access to electronic format (if available at all) as an add-on. *Preventive Veterinary Medicine*, published by Elsevier Science is available in libraries who have subscribed to "Science Direct," Elsevier's electronic journal database or to individuals who have a current print subscription and who have subscribed to Elsevier's "Science Direct Web Editions" service for an additional fee.

Databases

Databases can be categorized into those providing bibliographic information and those with statistical or numeric information. There is also an emerging trend to produce "metadata" or data about data. An example of this would be a database of other databases.

Several bibliographic databases have already been mentioned. In addition to the PubMed (http://www.ncbi.nlm.nih.gov/pubmed/) and CAB International (http://www.cabi.org) databases, veterinarians should be aware of Agricola, a database produced by the National Agriculture Library. Agricola is free to the public and accessible on the web at http://www.nal.usda.gov/. This database contains citations to journal articles, conference proceedings, books and, sometimes, book chapters, available at the National Agriculture Library in Bethesda, MD. It is especially useful for large animal medicine information.

The value of a database is dependent on the ability of the user to extract useful information from it. Given the broad scope of veterinary epidemiology, it will be left to the reader to determine whether or not a particular database fills an information need. The reader should remember that URLs for web sites change frequently. If the site listed is not found at the specific URL given, the URL for the homepage can be accessed and additional links can be followed from there. Also, veterinary medical topics are often found under the heading of **animal health**. The following is a short list of some numeric or statistical databases available to the public on the internet:

- The National Center for Health Statistics makes available an extensive list of health statistics databases at their web site at http://www.cdc.gov/nchs/products/pubs/pubd/hus/hus.htm.

- FedStats provides statistics on human health and demographics from more than 100 U.S. Federal agencies at http://www.fedstats.gov/ with links to statistics by topic or by agency.
- U. S. Department of Agriculture, Animal and Plant Health Inspection Services, Veterinary Services division web site at http://www.aphis.usda.gov/vs/ gives reports on cattle, horses, pigs, poultry, sheep, aquaculture, and wildlife. Reports are posted by the Center for Animal Health Monitoring, the National Animal Health Programs, and Emergency Programs divisions and includes research project results, general information, and fact sheets, as well as articles on current topics of concern.

The USDA also posts a web site for the National Agricultural Statistics Service at http://www.usda.gov/nass/ with publications, graphics, census of agriculture, statistical research and state information on U.S. agricultural product and markets. The site is searchable by keyword. This is only a short list of statistical and numeric databases available to the public. A Web search software, such as http://altavista.com or http://www.google.com, can be used to search for “numerical database” or “statistical database” These will retrieve an extensive list. Many university libraries have links to such databases, with notations on which ones are restricted to university users and which are open to the public.

Web Sites

A great deal of the information resources already mentioned are posted on the internet. In addition, veterinary epidemiologists should be aware of the links provided by NetVet at http://netvet.wustl.edu/. In the "Veterinary Resources" category, select "Specialties" to find "Epidemiology." Also, the links available under "Education" can be used to connect to veterinary colleges around the world and to discover what resources are available on the Web in the various departments teaching veterinary epidemiology courses. Information on zoonoses with links to many sources at the World Health Organization is also available:

- http://www.vetmed.wsu.edu/courses-jmgay/Epilinks.htm is an extensive list of epidemiology and evidence-based medicine web sites for veterinarians posted by John M. Gay, DVM PhD DACVPM ACE, of the College of Veterinary Medicine at Washington State University. Be aware that such sites posted by individuals are subject to change.
- "Virtual Rounds—Evidence-based Veterinary Medicine" found at http://www.cvm.uiuc.edu/courses/VP350/rounds/RoundsHome.htm posted by Dr. Ronald D. Smith, University of Illinois, is an informative site featuring analysis of cases seen at the University of Illinois Veterinary Medical Teaching Hospital.

- EpiVetNet is hosted by Dr. Dirk Pfeiffer, Royal Veterinary College, London, England, at http://epiweb.massey.ac.nz/. EpiVetNet probably links to the most extensive collection of specifically veterinary epidemiology information on the Web. This site also features a link to join a number of veterinary epidemiology— or general epidemiology—related internet discussion lists. A mirror site is located at Massey University's EpiCenter: http://epicentre.massey.ac.nz/. This site features links to several veterinary epidemiology software programs. Development of the EpiMAN software with versions for management of tuberculosis, foot and mouth disease, swine fever, and food safety is a project of EpiCenter Software Development Group and is described at this site.
- The Royal College of Veterinary Surgeons maintains a web site concerning evidence-based Veterinary Medicine at http://www.rcvslibrary.org.uk/ebvm.html, which features some of the previously listed links in addition to a bibliography of articles.
- The University of Glasgow and the University of Strathclyde in Glasgow, Scotland host a web site on Veterinary Informatics and Epidemiology at http://www.vie.gla.ac.uk/. This site features links to information on the research projects of the Veterinary Informatics and Epidemiology Group, a joint research group of these universities. A bibliog-

raphy of publications of members is mentioned previously.

- The web site of the Association of Teachers of Veterinary Public Health and Preventive Medicine at http://www.cvm.uiuc.edu/atvphpm/ is hosted by the University of Illinois, with Dr. Ronald D. Smith as webmaster. In addition to association-related information, there are numerous links to veterinary epidemiology software, online educational resources, and other related organizations. Links to the association newsletter and the online version of *Preventive Veterinary Medicine* are also featured.
- One general epidemiology web site worth listing is hosted by the United States Centers for Disease Control. The web site, called *Excite,* can be found at http://www.cdc.gov/excite. It features extensive links to all aspects of teaching epidemiology with an emphasis on human health as well as on-line journals.

People

It cannot be emphasized strongly enough that people are the best resource for **current** information. A research project or a drug trial can take months. Even case reports may not be up to date. A book is usually years in preparation and publication. Journal articles, although more current than monographs, still can take

months before appearing in print. After an article is submitted to a journal, it must go through the peer-review process and then wait in a queue with other articles accepted to be published. Unless one is a personal subscriber to a journal, or a frequent library visitor, existence of an article is usually discovered by searching a bibliographic database. Database services take on the average 6 months after publication to index an article. Articles from international journals take even longer. The National Library of Medicine, with the PubMed version of the Medline database, is making a concerted effort to speed the indexing process by entering abbreviated citations tagged "PreMedline" entries, with no abstracts. However, unless a relevant keyword appears in the title of these articles, they can be difficult to retrieve in a search.

Veterinary librarians are usually a good source for the latest information resources. A listing of members of the Veterinary Medical Libraries Section of the Medical Library Association can be found at http://filebox.vt.edu/vetmed/lib/vmls/. The group's web site is hosted by Virginia Tech University.

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Searching and Retrieving Information

Norma Funkhouser

Searching for Print Information

Monographs and journals published in the subject area of veterinary epidemiology can be located using databases maintained by university libraries, bookstores, and union catalogs (special library conglomerations of information sources). These resources are, for the most part, available using the internet. Use NetVet or the American Veterinary Medical Association (AVMA) membership

directory to locate a listing of veterinary libraries. Connect to their web sites and search their online catalogs for new books in this subject area. Search http://amazon.com or Barnes & Noble at http://www.bn.com for recently published works. Web sites of book publishers are also good resources for listings of new or planned book publications. OCLC (a library database resource) provides access, only through libraries, both public and academic based, to First Search, a huge union catalog of holdings of libraries from all over the United States. It is widely used by interlibrary loan departments as a resource to identify which libraries own which books and journals, but it can be searched by keyword to locate all books or journals in the database in a particular subject area.

General Searching Tips

VOCABULARY, VOCABULARY, VOCABULARY! When searching bibliographic databases for veterinary epidemiology information, vocabulary is critical! The veterinary literature is not indexed as carefully as the literature in human medicine, and the vocabulary is not as controlled. A bibliographic database is only useful if it can be easily searched and relevant citations retrieved.

PubMed, the publicly accessible Medline database posted on the web by the National Library of Medicine

at http://www.ncbi.nlm.nih.gov/pubmed/, indexes only about 65 veterinary journals. The indexing and vocabulary control is excellent, with all citations being assigned specific Medical Subject Headings (MeSH). However, it has only been in the past 10 years or so, at the urging of veterinary librarians across the country, that the indexing of veterinary journal articles has been as strict (see examples later).

CAB Abstracts, produced by CAB International, based in Reading, England is the premier bibliographic database for veterinary journal article information. However, CAB Abstracts is not available for free. Most university veterinary school libraries subscribe to CAB, and access can be obtained at those facilities. It is possible for an individual or a veterinary practice to subscribe to CAB through their web site at http://www.cabi.org/. However, it is fairly expensive. It is critical to be aware that CAB Abstracts uses British spellings in their indexing. Citations and abstracts from journals published in the United States are not changed to include British spellings, but the descriptive terms assigned to each article do use British spelling, for example, haemoglobin for hemoglobin, oestrus or estrus, and theatre for theater. In addition, the producers of CAB, on occasion, compose abstracts for articles that are considered important, published in journals that do not otherwise require an author-composed abstract. British spelling is used for these CABI

produced abstracts. Vocabulary in CAB is not strictly controlled. It is necessary to use a variety of synonyms to obtain good retrieval. Do not use just "dog" but include "canine" and "canis" and any plurals that may apply. A CAB Abstracts Thesaurus is published and available in most veterinary libraries. Also, the database uses "CABI codes" to index articles, but they are not strictly applied to all articles, especially older ones.

The same cautions apply to the Agricola database, from the National Agriculture Library. Vocabulary is not strictly controlled—synonyms should be used.

The search should be kept simple, using the broadest possible vocabulary terms and limiting retrieval after seeing how much information is available.

Example Searches

The following are some common types of questions asked in veterinary practice that are epidemiologic in nature. After each question, the search strategy is used to find the relevant citations listed. PubMed, the database to which everyone has access, is available at *http://www.ncbi.nlm.nih.gov/pubmed/*.

Question

Is it necessary to give antibiotics perioperatively in dogs or cats with uncomplicated orthopedic surgery?

SEARCH STRATEGY Start by selecting words from the question that are specific and unique—in this case **peri-operative**. Do not search a word using hyphenation—search for **perioperative**. Place limits of "animal" and "English language" on this search. All PubMed citations are tagged "human," "animal," or both. Search for the phrase orthopedic surgery. Search for **dogs** OR **cats**. No need to use feline or canine synonyms. The Medical Subject Headings for animals use their common name in plural form. Boolean connectors, such as **AND**, **OR**, **NOT,** must be in **UPPER CASE** when searching PubMed. Now display the search history and combine the retrieved sets by searching for #1 AND #2 AND #3. Remember to use the **#** sign before all set numbers.

- One article: Effect of perioperative prophylactic antimicrobial treatment in dogs undergoing elective orthopedic surgery. *JAVMA* 1999; 215:212–216.

Question

How well do heartworm test kits work in cats?

SEARCH STRATEGY Checking the Medical Subject Headings will not turn up an entry for "test kits." On a general question such as this, it is best to conduct a broad search for **heartworm** AND **cats**. If retrieval is less than 50 or 60 citations, it is better to scan them for relevance than to attempt to narrow the search further. See

Chapter 4 for additional suggestions. Adding additional terms may eliminate important articles.

- Several articles, including the main article: Performance of serologic tests used to detect heartworm infection in cats. *JAVMA* 2000; 216:693–700.

Question

How effective is bovine respiratory syncytial virus vaccine in cows?

SEARCH STRATEGY Use the specific phrase **bovine respiratory syncytial virus** (as it is not likely to be a Medical Subject Heading) AND **vaccine**. Because this question will probably be answered by a clinical trial, limit to that publication type. This search should also be run in the Agricola database from the National Agriculture Library at http://www.nal.usda.gov/ because PubMed does not index many large animal veterinary journals.

- Several articles, including the main article:

Milk production and reproductive performance in dairy cows given BRSV vaccine prior to parturition. *JAVMA* 1997; 210:1779–1787.

Question

Does continuing education change the way veterinarians and clients manage their herds (specifically dairy)?

SEARCH STRATEGY Search for the phrase **continuing education** combined with **herd management**. This search should also be run in the Agricola database from the National Agriculture Library at http://www.nal.usda.gov/since PubMed does not index many large animal veterinary journals.

- Two articles, including the main article: Effect of participation by veterinarians in a dairy production medicine continuing education course on management practices and performance of client herds. *JAVMA* 1996; 209: 1086–1090.

Question

How helpful are the terms used to describe prognosis in veterinary medicine?

SEARCH STRATEGY This is tough question. Consider that the plural of **prognosis** is **prognoses**, and use truncation in this search. The * is the accepted symbol in PubMed, so search prognos* to retrieve both singular and plural forms of the word. The phrase *veterinary medicine* has not been a medical subject heading for very long. If a search using veterinary medicine AND prognos* does not retrieve anything useful, do not give up! There may some older articles that will answer the question. Browse the MeSH headings, a selection in the sidebar of PubMed, to learn that some "see also" terms for

"veterinary medicine" include "animal diseases." Searching for animal disease* and prognos* retrieves some relevant citations.

- Several articles, including the main article:
  Usefulness of prognoses: qualitative terms vs quantitative terms. *JAVMA* 1985; 187: 700–703.

Question

How good are the feline leukemia virus vaccines at preventing disease in cats?

SEARCH STRATEGY Use the synonym *efficacy* for the phrase "how good are." Combine feline leukemia virus AND efficacy AND vaccine. If too many articles are retrieved, try limiting to English or review articles as a publication type. See Chapter 4 for additional ways to limit the number of articles.

- Several articles, including the main article: Immunogenicity and efficacy of a commercial feline leukemia virus vaccine. *JVIM* 1993; 7:34–39.

Question

Does *E. coli* antiserum prevent disease/death in foals?

SEARCH STRATEGY Remember to use full genus species names when searching bacterial organisms. Search

Escherichia AND foals AND antiser*. This search should also be run in the Agricola database from the National Agriculture Library at http://www.nal.usda.gov/ since PubMed does not index many large animal veterinary journals.

- A few articles, including the main article: Randomized controlled trial of effects of *E. coli* antiserum on serum immunoglobulin G concentration and morbidity and mortality rates in foals. *JAVMA* 1998; 212:1746–1750.

Searching the Internet for Information

Almost every search engine available on the internet has its own special characteristics and quirks. Some search engines search only the titles of web pages that have been indexed. Some search the entire text of a web page, or even the text of all the pages linked to an anchor page. Some web search engines are not really anything more than a directory of sites, categorized by interest. *Yahoo* is one such site. Complete up-to-date information on the latest developments in search engines, evaluations of retrieval, and descriptions of exactly how they work can be found at the Search Engine Watch site at http://www.searchenginewatch.com/. Information on how to evaluate information located on the internet can be found at Widener University's Wolfgram Memorial Library at http://

www2.widener.edu/Wolfgram-Memorial-Library/webevaluation/webeval.htm. The evaluation resources posted at this site are used extensively by librarians nationwide who teach courses on evaluating web information. If up-to-date information is important, the date a web page was posted should be checked.

4

Initial Evaluation of the Search Results

Three components are used to evaluate initial search results. First, the quality of the article must be determined. The quality is affected by the design of the study performed, as well as by the details of the particular study. Second, if the study is of reasonably good quality or if no other information is available, the important and useful results must be determined. The third component is to determine how or if the results can be used in the specific clinical setting.

In cases in which quite a large number of possibly useful articles are found by the search or when time is very

Box 4-1. Initial Screening of Articles

1. Is the article from a peer-reviewed journal? This will generally but not always result in higher quality studies.
2. Is the study sponsored by an independent granting agency or by the manufacturer of the product? Independent agencies may have more structure and control over the quality of the research and less bias than a manufacturer.
3. Is the treatment (or other factor being evaluated) readily available and within the price range of most of the clients in the practice?
4. If the study is of high quality, will the results cause a change from current protocols in the practice?

limited, some initial screening of the articles (Box 4-1) may be helpful to find the better articles quickly.

Quality of the Data

Assessing the quality of the article is addressed in Chapters 5 to 8 for each of the four common clinical questions: treatment and prevention, diagnostic testing, prognosis, and causation. The assessment at this stage depends heavily on epidemiologic principles and study design issues. A number of different summary numbers to describe the results are presented and explained. Several of these summary numbers can be calculated for more than one type of clinical question. Different study

designs may also be used for each common clinical question. For clinical questions that concern owner opinions, beliefs, or perceptions, more qualitative studies that are generally based on interviews or focus groups may be performed. A brief discussion of this type of study is in Appendix 1.

Use of Review Articles in the Practice Setting

Many kinds of articles may be considered to be review articles. In veterinary medicine, review articles are often considered to be a good starting point for an overview of a disease or health problem. But many articles mix opinions, beliefs, and data, and the quality of information depends on the expertise of the author. A **systematic review article** clearly describes where the information included comes from and separates fact, conjecture, and opinion. The articles included in the review are evaluated with an eye toward the quality of information and its generalizability. A high-quality systematic review can provide a clear summary of data that allows the reader to actually apply the facts to the patient. Some guidelines for this type of systematic review are in Box 4-2.

Meta-analyses are a special subset of systematic reviews. In the human medical literature, meta-analyses are found with increasing frequency. A meta-analysis summarizes the results of several studies,

Box 4-2. Key Elements in a Systematic Overview

1. Was a specific clinically relevant question addressed by the author?
2. Did the author describe how articles and information were included or excluded?
3. Did the author consider all the important sources of articles and information?
4. Were the articles or information included evaluated for the quality of information provided?
5. Could another author generate the same list of articles or information and come to similar conclusions?
6. Did the author make it clear whether or not there was a consensus from the articles or information included when determining the answer to the question?

which are performed in similar ways to address the same clinical question. The summary is accomplished by combining the numeric outcome data (such as odds ratios, relative risks, or median survival time) or by actually reanalyzing the different data sets from multiple studies to get an overall consensus of the results. Unfortunately, they are performed rarely in veterinary medicine, primarily a result of the lack of reasonable numbers of different studies focusing on the same problem and the wide variability of approaches among existing studies.

Determining the Design of a Study from an Article

The materials and methods section of an article provides the necessary information to determine the study design if the paper is well written and organized. The following steps provide guidance in determining the study design. The stated design in the article may not always be correct or complete!

1. Determine what the objectives of the study were. What was the exposure or outcome of interest for the primary objective? Create a sentence: The study examined the way the "something" effected/changed/led to "another thing." The "something" is the exposure, "another thing" is the outcome. See Chapter 5 for a discussion of what an exposure is in epidemiology.
2. Determine how the subjects received the exposure. If the authors or investigators controlled which subject got which exposure, then the study was experimental. These studies are **clinical trials** of some type. If the investigators just recorded the exposure, then the study was observational and more information is needed to determine the study design.
3. Decide if the study was retrospective, prospective, or some of each. Studies are **retrospective** if all of the events of interest have occurred at the time the project begins. Studies are **prospective**

if the outcome (and sometimes the exposure) has not occurred at the time the project begins. Occasionally, a study will be **ambidirectional,** in which some of the outcomes of interest have already occurred at the time the project begins but some occur after the project starts. By definition, clinical trials are prospective.

4. Determine how many groups of subjects there were. Were these groups distinguished based on their exposure status, their outcome status, or some other criteria. If there were two or more groups, then the study was analytical. If it was a clinical trial of some sort, then the study should have at least one new intervention and one comparison or control group. If the study was observational, and there was only one group, the study is descriptive (either a case report or case series). If there were two groups, move on to #5.
5. Determine how the subjects were chosen. There are three main ways subjects get chosen for observational, analytical studies: (1) they are selected because of their exposure; (2) they are selected because of their outcome or disease, or (3) they were convenient (all in one place at a particular time). If the subjects are selected because of their exposure status (e.g., surgery versus medical management of a particular problem) and then followed to determine if the dis-

ease develops, the study is a **cohort** study. If the subjects were selected based on their disease or outcome status (e.g., they had glaucoma or they were free of glaucoma) and their past histories explored to determine exposure, then the study is a **case-control** study. If they were selected because of some other characteristic or convenience and then classified as exposed, unexposed, diseased, non-diseased, then the study is **cross-sectional**. See Table 4-1 for a brief overview of study designs and the general quality of data they may provide, with all other things being equal. Note that a poorly done clinical trial can provide worse evidence than a well-done cohort study.

Useful and Important Results

If an article passes the initial screening and the more detailed evaluation for each type of clinical question, then the useful results must be identified. In some articles, these results are already calculated and displayed in a summary table. In other cases, the results are embedded in the text or must be calculated using information in the article. The practitioner must then be able to interpret quantities like median survival times, preventive fractions, relative risks, and others before applying the results to the patient at hand.

Table 4-1. Overview of Epidemiologic Study Designs

Study Design	Method of Including Subjects	General Type of Study	Strength of Evidence
Clinical trial	Chosen and assigned to treatment by investigator	Experimental	Strong
Cohort	Selected by exposure status	Observational	Moderate to strong
Case-control	Selected by outcome or disease status	Observational	Moderate to weak
Cross-sectional	Selected at one point or period in time	Observational	Weak
Case series >10 subjects	Selected due to same disease or treatment	Observational (no comparison group)	Very weak
Case Report ≤10 subjects	Selected due to same disease or treatment	Observational (no comparison group)	Very weak

Applicability of the Results to the Specific Practice or Patient

Determining whether or not the results may be applicable to the specific clinical setting requires a judgment call. Some considerations are listed in Box 4-3.

There are three areas to consider when deciding whether the patients or clients are different in important ways. First, biologic issues or "animal" factors should be reviewed. Are there differences between the patients at the clinic and those in the study based on the pathology or physiologic response? These differences may relate to severity of disease, concurrent diseases, and general prognosis. Are there differences in drug metabolism, immune responses, or environment that could impact the efficacy of the treatment in the clinic's setting? Are breed, gender, age, or species likely to be important considerations in treatment efficacy or the occurrence of

Box 4-3. Are the Results Applicable to a Specific Clinical Setting?

1. Are the patients or clients different in important ways?
2. How much could the patients be helped by this information?
3. Is there a good veterinary-client relationship, which includes information about client preferences, finances, ability to provide at home care (if applicable), and other nonmedical considerations that might limit the usefulness of this information?

adverse effects? Information about these topics can come from studies of disease pathophysiology in the laboratory or practice setting, information on the causative agent, pharmacokinetics data and other types of epidemiologic studies such as cohort studies, and case reports.

Second, economic and compliance issues, or "owner factors," should be reviewed. Compliance with the actual administration of the treatment or with required monitoring may be influenced by the physical disabilities, education level, and knowledge base of the owner, as well as other events in the household or on the farm and by the relationship to and value of the animal. Good client communication is critical to assess the likelihood of treatment acceptance and success.

Third, access to the necessary equipment, services or information on the part of the practitioner may also limit treatment choices ("veterinary factors"). In treatment of idiopathic epilepsy with phenobarbital, therapeutic drug monitoring is highly recommended. However, availability, turn-around time, and cost may limit this resource. Accurate information on the frequency of adverse effects from the treatment may not be readily available, particularly if the treatment is new and has not been used in large numbers of animals. Estimates of the likelihood of negative events from not treating or pursuing another treatment may influence the owner's decision.

If the patients and clients are similar enough, the next question is to decide if the results are helpful enough to try. The extent to which a particular treatment, test, or piece of information from the article can help patients can be assessed partly by the measures reported in the results. The many different types of measures are discussed in the sections on each type of clinical question.

The assumption is made that a veterinary-client-patient relationship has been established to some degree for patients seen in the practice. Open and complete client communication is crucial when making difficult decisions, especially if the supporting data are limited or difficult for clients to understand.

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5

Making Decisions about Treatment and Prevention

There are three main reasons why veterinarians recommend treatments: to prolong life, to prevent future disease or injury, or to improve the quality of life for the patient and the client. The clinical questions that focus on treatment choices and preventive measures include the following topics:

1. Which antibiotic (or other medication) is more effective for a specific problem?
2. Is a medical or surgical approach best?
3. How effective is a vaccine?

4. Does a specific flea or other product prevent or control infection or infestation?

Treatments or preventive measures that are evaluated are commonly called **interventions**.

Quality of the Information

A **clinical trial** is the best study design to address the questions about treatment or prevention. A clinical trial is a prospective study in which the investigator controls which subjects enter which group (two or more groups may be used). Experiments similar to clinical trials may be conducted in the laboratory setting in which not only the intervention is controlled but also the environment. Clinical trials in the animals' natural environment are sometimes called **field trials**. Here, the investigator has control over the intervention assigned but has little or no control over the general care and environment of the animals.

The **subject** is the person, animal, or unit of interest (such as herd, pen, kennel) that is selected to be in the study. **Assignment** is a term used to describe how the factor or characteristic of interest is allocated to the subjects. The factor under study is commonly referred to as the **exposure** for studies of etiology and as the intervention for studies of efficacy including prognosis.

Randomization is a process by which each animal is assigned to one of the groups using a system that is not

influenced by the beliefs or preferences of the investigator. Tossing a coin is often considered to be the classic random process. Computer-generated random numbers (most spread-sheets can do this) or a printed random numbers table can also be used. Randomly assigning patients to a group helps even out potential differences between groups (particularly for factors that are not known to be important or cannot be easily measured) because these potential differences are also randomly scattered between groups. Assigning patients to groups based on day of the week, order that they arrive in the clinic or are run through the chute, or by ear-tag number is not random in the statistical sense referred to here. Depending on the method, there may be considerable bias introduced. For example, if the first 20 cattle to go through the chute get antibiotic A and the second 20 get antibiotic B, the two groups of cattle are not likely to be comparable in important ways. The last 20 maybe the sickest (thus slower to get to the chute), the oldest (thus more wary about the chute), or in some other way systematically different from the first 20 cows.

A **control group** is used as a baseline to show what would have happened without the intervention of interest. Control groups may have placebo medications or sham surgeries, but in general, patients in control groups should be treated with the current best treatment option. The control group should be as similar as possible to the exposed or treated group except for the

exposure or intervention being investigated. This means that extraneous variables that might also influence the outcome (**confounding variables**) are eliminated from the study or divided evenly between the intervention and control groups. Common potential confounding variables are age, breed, sex, and species. Control groups should be concurrent, that is, selected and assigned at the same time as the intervention groups. The importance of control groups and the possible complexities of the use of placebos can be seen in the example of a double-blinded, placebo-controlled crossover study that evaluated evening primrose oil as a treatment for atopy in dogs.[1] A **crossover** study means that each dog receives each treatment in a specific order. Because the authors also included a placebo treatment, they were able to uncover an apparent improvement in clinical scores (based on pruritus, erythema, edema, scaling, and coat condition) in both the placebo and treated groups during the first part of the study. When the dogs that originally received the primrose oil were switched to the placebo, their scores deteriorated, whereas the dogs that were switched to the primrose oil continued to improve. Based on the discussion, although the owners and investigators were blinded to the treatment group, the clinician assigning the scores was not. So there are three possibilities for the improvement of the dogs on placebo in the first part of the trial. First, it is possible that there was a placebo effect on the clinician, which is a

concern for outcome measurements that are subjective. Second, the placebo (olive oil) had some unexpected effect. Third, there were effects of season or environment during the time of the first treatments. This was possible because most dogs began the study during late summer and autumn, which often is a time of decreasing clinical signs in England. The authors tended to believe the third possibility based in part of the plasma phospholipid profiles. The findings of this study illuminate some of the difficulties inherent in clinical trials on owned animals with subjective outcomes.

In rare situations, a **historical control group** may be used. This is only appropriate if the course of the disease is predictable and well documented, and there are compelling reasons not to use a concurrent group due to ethical considerations or occasionally financial constraints. In a study evaluating the treatment of generalized demodicosis in adult dogs using milbemycin oxime, no concurrent controls were used.[2] The authors justified this by indicating that 24 of the 26 dogs had been treated aggressively and unsuccessfully before entering into the study (the other two had had demodicosis for 2 years), no reports of spontaneous resolution of the disease had ever been published, and no other acaricidal treatment was used during the study.

Blinding refers to keeping knowledge about which group the subject was assigned to secret, whenever this is

possible. Blinding is sometimes referred to as masking. Single blind studies prevent the owners or caretakers from knowing intervention assignment. Double-blind studies also keep the clinician responsible for clinical care and assessment unaware of intervention group. Triple blinding includes blinding of the owner, the clinician, and the investigators doing the analyses and handling the data. Although blinding is not always feasible (comparing medical vs surgical effects, for example), it will strengthen a study. Blinding is particularly important when the end results of the study tend to be more subjective.

The **outcome** is the endpoint of the study as defined and measured by the investigators. It may be referred to as the event of interest. It should be explicitly defined in the material and methods section of the manuscript. Sometimes the outcome is an intermediate or **surrogate event** such as a change in laboratory tests or tumor size rather than the actual clinically important event. These surrogate events are usually used because of time or costs considerations but can be misleading if they do not directly correlate with the clinically relevant outcome. Whenever possible, the actual clinically relevant endpoint should be used such as survival, recovery, relapse, return to function, because these are the truly important outcomes in the practice setting. For example, a randomized clinical trial on passive immunoglobulin transfer in dairy calves

compared colostrum to three commercial colostral-supplement products.[3] The level of IgG 24 hours after birth was used as one endpoint, but the authors also evaluated disease occurrence in each of the four groups for the first 30 days of life. This latter endpoint is a much more clinically relevant outcome. One comment about the article: The authors referred to disease frequency as disease prevalence, but the calves included seemed to be healthy at birth. Therefore, the disease frequency was likely incidence, in which calves had newly developed and diagnosed diseases. See later in this chapter for a discussion of incidence and prevalence. A similar study of dairy cows evaluated bovine respiratory syncytial virus vaccine and its effect on milk production and reproductive performance, as well as health problems associated with the virus for the outcomes.[4] This was particularly important for this vaccine because the disease in adult cattle is often mild or subclinical, and the cost-benefit analysis of vaccine use needed to include its effects on lactation.

The best clinical trials have a concurrent control group, random assignment of subjects to the different groups, and blinding (Box 5-1). They also have relatively similar groups receiving the interventions at the beginning and complete follow-up data on all the patients who entered the study. The more “yes” answers to the questions in the table, the better the study and the evidence provided.

Box 5-1. Key Elements for Studies of Clinical Trials of Treatment or Prevention

1. Was there a concurrent control group?
2. Did the control group receive the current best intervention rather than placebo (if appropriate)?
3. Were the subjects randomly assigned to the groups?
4. Were the groups similar at the beginning of the trial?
5. Was there blinding (single, double, or triple) to intervention assignment?
6. Was there relatively complete follow-up of all subjects (>80%) that entered the trial?
7. Were the results in the different groups relatively large and clinically important?
8. Was a formal (and appropriate) statistical analysis performed?

A 1999 article on perioperative antibiotics for dogs undergoing elective orthopedic surgery provides an example of a well-designed clinical trial that was also well written.[5] All of the 126 dogs that entered the study appear to have completed it. The authors used sample size calculations to determine that 201 dogs would be needed to detect a difference in infection rate of 4% (based on another study). After just over half of the dogs were enrolled, the infection rate in the saline group was more than 15% (much higher than in either antibiotic group) and the decision was appropriately made to end

enrollment on ethical grounds. When the two antimicrobial groups were combined, there was a statistically significant lower rate of infection in those groups compared with the saline group. However, there was not a significant difference between antimicrobials. For the cefazolin group, 3/48, or 6.3%, developed infections; for penicillin 1/43, or 2.3%, and for saline 5/35, or 14.2%, developed infections. None of these percentages were significantly different at $P<0.05$. However, an infection rate of 14% (compared with 3% to 6%) would likely be considered clinically important. Because of ethical concerns in using a saline control, too few dogs were included in the study to find statistically significant differences at the conclusion of the data collection. The authors discussed this in detail and provided some alternative statistical ways of looking at the results. Overall, the results were compelling.

Other Study Designs for Evaluating Treatment and Prevention

When a clinical trial is not available to assess treatments or preventions, other study designs may be used and are found much more commonly in the veterinary literature. The study designs with a control group that would most commonly be used for treatment or prevention include cohort or case-control studies. The primary limitation for **cohort studies** is due to the fact that

assignment to intervention group is not under the control of the investigators. Typically, which intervention the animal receives is based on the preferences or experiences of the clinician, on the severity or stage of disease, or on the preferences or finances of the owner. Any of these reasons can seriously undermine the usefulness and quality of a study to the point that it is not worth reading. For example, an article on two different combination interventions for vaccine-associated sarcomas in cats used a ambidirectional cohort design.[6] Cats were identified using the medical records. Both groups of cats received surgery and radiation, whereas one group also received doxorubicin. There were seven cats in the surgery and radiation group, and 19 in the group that included doxorubicin. The inclusion of doxorubicin was made based on the clients' choice, even though it was recommended for all cats. Additional serious limitations included (1) short follow-up of some cats (less than 3 months) because of the conclusion of the study; (2) differences in numbers of previous surgeries for the tumor among the cats; (3) differences in radiation dose and protocol; and (4) small sample size, which precluded any statistically significant findings. (The authors calculated the power of the various analyses to be between 5% and 18.5%.)

Case-control studies are useful for rare outcomes but are nearly always retrospective. Therefore, the kind and quality of information available about the

intervention is uneven at best and missing or completely wrong at worse. In veterinary medicine, case-control studies are rarely used for intervention evaluations.

Most commonly, **descriptive studies** are published in the veterinary literature. These observational studies do not have a control group and provide poor evidence of efficacy. A case report (<10 subjects) or case series (≥10 subjects) includes animals with some similarity of interest. Therefore, to make any use of these designs for evaluating efficacy, the reader must be very knowledgeable about the usual course of disease and response to intervention, the source of the patients in the study, and reasons for intervention choice (like the cohort study). Descriptive studies are appropriate for a very rare or new disease or unusual presentation of a more common disease. They may also be helpful in describing the usual clinical course of some exposure or disease. At times, making the distinction between a case series and a retrospective cohort study can be difficult. In general, if the objective of the study was a comparison of different exposures and animals were included based on the exposure, then the study was a cohort study. However, regardless of the specific study design, the same serious limitations apply to a retrospective cohort and a case series as designed to evaluate an intervention. An example of a case series that draws conclusions about treatment efficacy is an article concerning nonhealing ulcers

in cats.[7] This retrospective study reviewed the medical records of cats diagnosed with non-healing corneal ulcers (29 cats with 31 ulcers in 9 years). Treatments compared were débridement, débridement with grid keratotomy, and superficial keratectomy. Because of the study design, treatments were not randomized and no blinding was used. Two cats were treated with superficial keratectomy at the owners' request. The ages, breeds, and sexes of the affected cats were given for the 29 cats. No definition of nonhealing ulcer was provided, although ulcers with a loose lip of epithelium were included. Limitations of this study for drawing conclusions about treatment included (1) some cats had previous histories of ulcers; (2) no information on why a given treatment was used (except for superficial keratectomy); (3) 14 eyes (unknown number of cats) were lost to follow-up before healing; (4) variable topical treatments, including different antibiotics and in some cases steroids; (5) use of soft contact lenses in some cats; and (6) healing time was given as a mean of 5 weeks for all cats, 30 days for débridement alone, 6 weeks for keratotomy, and 2 weeks for the keratectomy cats. The time to healing was not normally distributed based on the ranges given so medians should have been reported. Because of the short time to healing of the débridement-alone group and the simplicity of this treatment, this group might have been the least severely affected; (7) no statistical analysis was performed. Because of

these limitations, no real conclusions about treatment are possible.

Other Sources of Information

Other common sources of information on treatment and prevention are continuing education seminars and the manufacturers of the product. Information presented in continuing education seminars is usually based on the experience of the presenter. There may or may not be data to support the expert's opinion, and the expert may very well practice in a different sort of setting than the general practitioner. In situations in which no good current therapy is available or when the expert is reporting the results of a well-conducted clinical trial or critical review of available data, continuing education may provide data of reasonable to excellent quality.

Pharmaceutical companies may or may not have hard data to present. Package inserts usually do not provide any kind of evidence for efficacy. A key question to consider is: How does the new product compare to the existing products? Companies may or may not have or release information comparing their new product with the competitor, which is really the information needed to make informed decisions. Data collected on projects performed by the company on the company premises are rarely peer reviewed and may be biased.

Results from Clinical Trials

Typically the outcomes from a clinical trial are summarized using some measure of incidence. **Incidence** is the number of new events in the population or group over a particular time period. The event may be death, recovery, occurrence of a disease, relapse, a particular sign or clinical finding, or any other specific measurement of interest. The key element here is **new events**. Therefore, the animal must be free of that event at the beginning of the study, so that the event developed after the intervention groups were formed and intervention initiated. This means that there will always be at least two assessments for the event of interest, one at the beginning of the study and one later in the study to confirm or deny the event occurred while the patient was undergoing intervention. If the study measures the frequency of existing cases (both new and previously diagnosed or occurring), then the measure of frequency is **prevalence**. Two common types of incidence are cumulative incidence and incidence density. **Cumulative incidence** is the number of individuals that have the event during the study period divided by the number of individuals that could develop the event at the start of the study (sometimes called *population at risk*). For example, in a randomized clinical trial on the efficacy of *Escherichia coli* antiserum in neonatal foals, 30 of 138 treated foals became ill with some health

problem.[8] This corresponds to a cumulative incidence of 22%.

Incidence density has the same numerator as cumulative incidence but is divided by the sum of the length of time of observation for all individuals before the event occurred. This denominator is often measured in animal-years at risk or animal-months at risk. This measurement is used infrequently in veterinary medicine. However, it can be extremely useful in a setting in which the time the animals were included in the study varied, as would happen if animals were entered into the study across a 2-year time period and the study ended 3 years after the first animal was included. One example in the literature is a randomized clinical trial of a new feline leukemia vaccine in a communal cat shelter setting.[9] Because cats were added to the trial across a 4-month period and cats died during the trial (therefore, had less than the anticipated 1 year of exposure to positive cats), incidence density was used in addition to cumulative incidence. The incidence density was defined as the number of cats with the outcome (persistent viremia) in the group (vaccinated or placebo) divided by the number of months the cats had been at risk (exposed to the positive cats after entering the study). The incidence density in the vaccinated and placebo groups were then used just as a cumulative incidence in comparing groups and calculating a preventive fraction.

To compare the incidence in the two groups, several measures are used. **Relative risk** (RR) is the incidence in the treated group, divided by the incidence in the control or standard treatment group. RR greater than one indicates that the event occurred more often in the treated group than the control. RR of less than one means that it occurred less frequently in the treated group than the control or that the treatment is protective for the event. A RR of one means that there is no difference in the incidence between the two groups and that there is no association or relationship between the event and the intervention groups. However, a measure of statistical significance is needed to tell if the RR is far enough away from one to be truly increased or decreased. *P* values or confidence intervals can be used to make this decision. In the previous neonatal foal example, the incidence of infectious illnesses in treated foals was 21 of 138 (8%) and in control foals was 27 of 133 (10%).[8] The relative risk is 8%, divided by 10% or 0.8. Although this RR is less than one, implying a protective effect, the difference in cumulative incidences was not statistically significant based on the *P* value. Therefore, this relative risk of 0.8 is not significantly different from one, and there is no difference between the treated and control groups in the frequency of infectious illness. For the example from the study on different colostral-supplements, the incidence of illness for one product was nine of 13 calves (69%) and for another 12 of 14 calves (86%).[3] The relative risk

of illness would be 0.8 when comparing the first product with the second one. Because these cumulative incidences were significantly different from one another, this relative risk is significantly different from one. Therefore, the first product provides significantly more protection (about 20% more) against illness than the second product (although neither was as effective as natural colostrum).

Another measurement that can be used is the **attributable risk** (AR), also called the risk difference. This measure is calculated by taking the incidence in the treated group and subtracting the incidence in the control group. This difference is the change in the frequency of the event attributable to the intervention. A positive difference indicates that the incidence is greater in the treated group, whereas a negative one means that the incidence is greater in the control group. The **absolute risk reduction** is used in the human literature and is the opposite difference (control minus treated). The inverse of this quantity is the **number needed to treat** (NNT). The NNT is how many patients would need to be treated with this intervention to give one more patient a positive outcome. See Table 5-1 for example calculations.

Another related quantity is the **RR reduction.** The RR reduction uses the control incidence minus the intervention incidence and divides by the control incidence. This is commonly referred to as the **preventive**

Table 5-1. Calculations of Common Measurements in Clinical Trials Using an Example Clinical Trial of Two Feline Leukemia Vaccines

Measurement	Formula*	Example Calculation	Interpretation
(CI)	Number with new event/population at risk	11/30 = 0.37 (vaccinates) 17/20 = 0.85 (controls)	37% of the vaccinates became persistently viremic during the study
RR	CI treated/CI control	0.37/0.85 = 0.43	The vaccinates were less than 1/2 (0.4 times) as likely to develop viremia compared with the controls.
AR	CI treated–CI control	0.37–0.85 = -0.48	About 1/2 (0.48) of the decrease in incidence of viremia is due to the vaccine.
Number needed to treat	1/AR	1/0.48 = 2	For every two cats vaccinated, one will be prevented from becoming viremic.
RR reduction (preventable fraction)	(CI control–CI treated)/ CI control	(0.85–0.37)/ 0.85 = 0.56	The vaccine reduces risk of disease 56% after accounting for natural immunity.

CI, Cumulative incidence; *RR,* relative risk; *AR,* attributable risk.
*These calculations also work for incidence density as a measure of incidence. Similarly, the intervention may be considered to be the exposed group and the control the unexposed group.

fraction in vaccination studies in which the vaccinated group is the intervention group. This measure provides information about the proportional decrease in the event by taking into account the incidence in the control group. It does not give any idea of the absolute size of the change in risk. For some other, less commonly used, measurements see Thrusfield.

Using data from a clinical trial of several feline leukemia vaccines, each of these measurements was calculated (see Table 5-1).[10] In this example, the event of interest is viremia and all kittens were virus free at the start of the study so that the viremia is newly acquired, thus measuring the incidence of viremia. Thirty kittens were included in the vaccinated group (treated) and 20 in the control group.

To illustrate further the differences between the measurements, Table 5-2 provides some hypothetical data. Notice that the relative risk and the preventable fraction are the same for all levels of incidence. However, the level of preventable viremia that can be attributed to the vaccination has become trivial (less than 5% of cats are protected by the vaccine), and therefore, the number of cats needed to vaccinate to prevent viremia in one cat has skyrocketed. Although these numbers seem a bit unrealistic for a vaccination study and are really used here to make a point, in feline leukemia vaccine testing, some studies do have very low incidences of viremia.

Table 5-2. Hypothetical Data to Illustrate the Effect of Incidence on the Different Measurements Used in Clinical Trials

Source Data	Incidence Controls	Incidence Vaccinates	Relative Risk	Attributable Risk	Number Needed to Treat	Preventable Fraction
Original study	85%	37%	37%/85% = 43%	37%–85% = –48%	1/48% = 2	(85%–37%)/85% = 56%
Hypothetical moderate	8.5%	3.7%	3.7%/8.5% = 43%	3.7%–8.5% = –4.8%	1/4.8% = 21	(8.5%–3.7%)/ 8.5% = 56%
Hypothetical low	0.85%	0.37%	0.85%/ 0.37% = 43%	0.37%–0.85% = –0.48%	1/0.48% = 208	(0.85%–0.37%)/ 0.85% = 56%

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6

Making Decisions about Diagnostic and Screening Tests

A **diagnostic test** is anything that provides data about the health or illness of the patient. Diagnostic tests include the usual laboratory blood and urine tests, as well as imaging techniques (radiography, ultrasound, computed tomography scans, magnetic resonance imaging [MRI]), physical examination findings (temperature, auscultation), and history (diet, environment, travel). All of these tests can be formally evaluated for their accuracy and precision. For example, the sensitivity and specificity of physical examination and lymph node aspirates were evaluated

in the diagnosis of metastatic cancer in dogs and cats.[1] Unfortunately, in veterinary medicine, many tests have not been evaluated as often as in human medicine, and there are no central locations (either written or electronic) that summarize existing data on diagnostic tests.

Diagnostic tests are use to hone in on the specific cause of the disease process in patients with clinical disease. Diagnostic tests may also be used to determine the severity of disease, to predict prognosis, to determine the likely response to treatment, and to monitor the patient's actual response to treatment. Screening tests are used in apparently healthy patients or patients without clinical signs of the disease of interest to look for subclinical disease. Screening may also be performed to find patients at high risk of developing a disease. New tests may by evaluated because there is no current test or because the current test is expensive, risky, invasive, painful, or not very good. The same test may often be used in both a diagnostic and screening setting (see later in this chapter and Table 6-1 and Box 6-2 for information on screening tests). But it is important to recognize that the set of patients seen in each situation will be different and the accuracy of the test will likewise vary. It is relatively simple to tell a normal sound horse from a horse with neurologic disease based on physical examination. It will not be easy to distinguish a horse with neurologic signs from equine protozoal myeloencephalitis from a horse with other kinds of central nervous system disease.

Table 6-1. Calculations for Test Accuracy and Application

	Disease+ (D+)	**Disease– (D–)**
Gold Standard Results	*a*	*b*
Test+ (T+)	true positive (TP)	false positive (FP)
Test– (T–)	c false negative (FN)	d true negative (TN)
a + b + c + d = N	a + c	b + d

Prevalence = a + c/(a + b + c + d) = D+/ N

Sensitivity = a/(a + c) = TP/D+

Specificity = d/(b + d) = TN/D-

PPV = a/ (a + b) = TP/T+

NNV = d/ (c + d) = TN/T–

Likelihood ratio for a positive test = a/a + c / b/b + d = sensitivity/(1 – specificity)

Likelihood ratio for a negative test = c/a + c / d/b + d = (1 – sensitivity)/specificity

General likelihood ratio for any particular category of results= (likelihood of a particular test result in someone with disease)/(likelihood of the same test result in someone without the disease)

Because the methods and issues in evaluating diagnostic and screening tests are similar, the discussion about tests includes both types unless otherwise indicated.

Tests are good when they consistently yield a positive result in patients with the disease or disorder and negative

results in patients free of the disease. The measurements that quantify how good a test is are false positive and false negative rates, sensitivity and specificity, and positive and negative predictive values or likelihood ratios. These measurements reflect the **accuracy** of the test. The test should also be **consistent** (sometimes referred to as reliable, repeatable, or reproducible). This means that if the test is repeated on the same sample or patient, the same result will be found. Consistency also includes similar results if the test is performed by different technicians or veterinarians, as well as laboratories. This type of consistency depends on the experience of the person performing the test and the reaction of the test to variations in the environment and the sample.

To determine the accuracy of a test, the true health status of that animal must be determined. The gold standard is the current best "test" (or combination of information) that separates animals with the disease from animals without the disease of interest. Often necropsy or surgery are used, but the gold standard may include a combination of information about history as well as other types of tests. Box 6-1 contains the key elements for a good article on testing. The more "yes" answers, the better the article. Sometimes two tests are compared when neither one is a gold standard. See Appendix 2 for a brief discussion of this topic.

Screening programs are common in human medicine but less so in veterinary practice. Still, several common programs can be found. A good example is

Box 6-1. Key Elements for Studies on Diagnostic Tests

1. Was an appropriate gold standard selected based on the best available tests?
2. Was the new test run and compared with the gold standard (or best available test) blindly in all subjects? This also means that the new test was not part of the gold standard.
3. Were the subjects included in the study representative of the group in which the test would be used in practice? This includes the severity or stage of disease, species, concurrent diseases, etc.
4. Were the exact instructions for conducting the test described or available?
5. Was a direct comparison of the gold standard and new test made using false-positive and false-negative rates, sensitivity and specificity, and positive and negative predictive values, or likelihood ratios?
6. Does the test work well in distinguishing the difficult to distinguish patients?

screening for heartworm disease in dogs. See Box 6-2 for guidelines for good screening programs. One caveat for item 2 in this table is that for diseases with very long periods of time between potential disease detection and clinical problems, there will be many animals diagnosed early with the disease that will not develop clinical signs for many years. For some animals, their age or lifestyle will preclude their ever developing the clinical disease, making screening a waste of effort and money for their

Box 6-2. Considerations for Developing and Using Screening Programs in Practice

1. The disease is serious and severe.
2. The disease has a relatively long asymptomatic period, which means that the natural history of the disease is known.
3. The disease is common.
4. A treatment (or prevention) exists that will improve quality of life or survival and is acceptable to the client.
5. The treatment will be more effective if begun during the subclinical period of disease.
6. The test is accurate, precise, and available.
7. The test is safe, easy to perform, inexpensive, and acceptable to clients.

owners. A poorly designed and evaluated screening program can be harmful if (1) patients are diagnosed with a disease they do not have, causing additional testing, cost, and client anxiety; (2) the treatment has not been shown to be beneficial for patients in the subclinical or early stages of disease; or (3) the client is unable or unwilling to pursue recommended treatment in spite of an accurate diagnosis causing guilt, stress, and possibly ill-advised home remedies.

Results for Diagnostic Tests

The accuracy of a test is measured using **sensitivity** and **specificity**, which are a function of the number of

false-negative or false-positive results, respectively. The sensitivity and specificity of a test are considered to be a property of the test. However, they vary depending on a number of factors, including severity or extent of disease, standardization of the test technique, and appropriateness of the population in which the test has been evaluated. The **sensitivity** of a test is the ability of the test to give positive results among animals that truly have disease. The **specificity** of the test is the ability to give negative results among animals that are truly free of the disease. To decide whether an animal is truly free of the disease of interest (the true situation), a **gold standard** test or combination of tests is used. The gold standard should be independent of (i.e., not related to) the other test being evaluated. Often necropsy, histopathology, or surgery are used as a gold standard. However, for some diseases, it is difficult or impossible to know the true disease situation. The **prevalence** or **pretest probability** of disease estimates how likely is it that the animal has the disease before the test is used. These estimates commonly come from clinical experience, the experience of others, the practice database, or articles about the prevalence of the disease. Prevalence varies depending on the geographic location, type of practice, and sorts of patients that are seen. The **post-test probability of disease** is the best estimate of how likely the animal is to have the disease after the test results are known.

There are many reasons for tests to be inaccurate. The lack of accuracy may be due to a high number of false-positive tests (leading to a low specificity) or a high number of false-negative test results (leading to low sensitivity). In general, the reasons fall into four main categories: (1) the measurement being used to indicate that disease is present (e.g., antibody, heart murmur, and glucose level) is also found in some portion of healthy animals or in animals with other similar diseases; (2) there is individual animal variation in expressing what the test measures; (3) there are problems with the sample itself in collection, storage or processing; and (4) there are problems with actually performing the test, including level of experience of the person, the level of skill and training required to perform the test, and the complexity of the test itself.

Although sensitivity and specificity are important to know, applying the test in the clinical setting results only in a positive or negative result. So if the test comes back positive, how likely is it that the patient really has the disease of interest? This question is answered by the **positive predictive value** (PPV), which provide an estimate of the proportion of animals testing positive and having the disease. In the situation with a negative test result, a **negative predictive value** (NPV) indicates how likely it is that the animal is truly free of disease. They are usually presented as percentages. Table 6-1 summarizes the formulas for calculation of these numbers.

Table 6-2. Example Data for Calculations of Sensitivity and Specificity

	Disease +	Disease –
Test +	44.5 (or 45)	209
Test –	5.5 (or 5)	741
TOTAL: 1000	50	950

Some advice is helpful when calculating these values from an article or drug insert: Always lay out the 2 × 2 table in the same way. Doing this means that sensitivity is always the first column of data, specificity the second column, and predictive values will always be calculated horizontally. See Appendix 3 for a step-by-step process to work from data in articles.

An example of this process is shown in Table 6-2. Using a heartworm antigen test for cats, the sensitivity is 89% and the specificity is 78%. In general, heartworm prevalence in all cats is about 1/10th that of dogs. In Texas, a prevalence of 5% is a reasonable pretest probability.

Because predictive values are calculated horizontally and use information that depends on the prevalence of the disease, they are affected by changes in prevalence. For this example the PPV = 45/ 45 + 209 = 0.18 or 18%. This means that a positive test result is correct only about 18% of the time (not very often!). The NPV is 741/741 + 5 = 0.99 or 99%. This means that a negative

test result is correct 99% of the time, with a prevalence of 5%. Using the same sensitivity and specificity, if the disease is rare (the prevalence is low), most animals will be negative and only a few will be positive. This means that a negative result is very likely to be true negative (TN), whereas a positive result is more likely to be a false positive (FP). So, in many parts of the country with lower prevalence of heartworm disease in cats, the NPV will be even higher and the PPV even worse. Conversely, as the disease becomes more common (the prevalence is higher), then the PPV will go up and the NPV will go down. How much the predictive value changes depends on the sensitivity and specificity, as well as the range of prevalence for the disease. These relationships are true for all tests.

In addition to the trends for NPV and PPV due to prevalence, tests with very high sensitivity or specificity also tend to influence PV in systematic ways. For tests with very high specificity (few FPs), positive test results will have a higher PPV than for tests with lower specificity. This means that in the extreme case of 100% specificity, PPV will always be 100% (TP/TP + 0 [FP]). So highly specific tests will be better for ruling in a disease (high PPV) compared with tests with lower specificity. The opposite is true for tests with high sensitivity. For tests with 100% sensitivity, there are no FNs, and NPV is 100%. Therefore, highly sensitive tests are good for ruling out a disease—a negative result can be trusted. In

general, tests never really show 100% sensitivity or specificity, but these trends will hold true for test results.

How does one decide what is the patient's pretest probability of having the disease? Think about this as the prevalence of the disease in a group of animals similar to this patient. This estimate of prevalence is based on personal experience, practice data, laboratory records, or if necessary, colleagues' experiences, if that is all that is available. If there is a range of possible pretest probabilities, the predictive values can be calculated for the high and low end to see if the conclusions about the test results will change in important ways.

Whenever the test has a continuum of results (like clinical chemistries), a decision will be needed about what is clinically normal and what is abnormal to calculate sensitivity and specificity. The selection of a cut-off point for normal depends on the relative importance of sensitivity vs specificity. A cut-off point can be defined that excludes all ill animals. In that case, there will be no false-negative results and a high specificity. However, the trade-off will be an increase in false-positive results and a low sensitivity. Conversely, a cut-off point that excludes all healthy animals will have no false-positive results and a high specificity. This trade-off between sensitivity and specificity will always be present, and the cut-off will usually depend on the specific application of the test. However, if likelihood ratios (discussed later in the chapter) are used, then a set of ranges for the test result can be

determined instead of just a single cut-off and the likelihood ratio for each range of values can be calculated.

Another measurement that may be used with tests that take on a spectrum of values is the **receiver or response operating characteristic curve** (ROC curve). This is a graphic method of summarizing the accuracy of a test. The curve is made by plotting the sensitivity on the vertical axis and the false-positive rate (1-specificity) on the horizontal axis. For each possible cut-off point, the sensitivity (true-positive [TP] rate) and FP rate are calculated and graphed. The **ROC curve value** is the area under the curve. A ROC value greater than 80% is indicative of a good test. The point on the ROC curve that is closest to the upper left corner gives the best combination of both sensitivity and specificity. The ROC curve can also be used as a summary measure for comparing tests: the test with the largest area under the curve (which would have the curve closest to the upper left corner) is the most accurate test.

Likelihood Ratios

Sometimes **likelihood ratios** (LR) are used instead of predictive values. The advantages are that they are not affected by prevalence because they depend only on sensitivity and specificity, they can use multiple cut-off points for a test result on a continuum (where the results are continuous and where higher values make disease

more likely), and they can be used to calculate actual probability of a disease on the differential list if the pretest probability is known. The obvious disadvantage is their calculation and interpretation. They are rarely used in the veterinary literature.

A positive likelihood ratio is the probability of a positive test among the subjects with the disease divided by the same probability in the non-diseased subjects. Similarly, a negative likelihood ratio is the probability of a negative test in diseased subjects divided by the probability of a negative test in nondiseased subjects. If the test has multiple levels and cut-off points, then a likelihood ratio is calculated for each level where the numerator is the probability of a test result in that range of values for a diseased subject divided by the same probability among the non-diseased subjects (see Table 6-1). In one example on the evaluation of a ELISA for bovine paratuberculosis, the potential usefulness of LR is demonstrated.[2] A table in the article summarized the optical densities (OD) obtained from an ELISA test with the corresponding LR for each range of OD for either infection by the organism or isolation of the organism in fecal samples. Even a small increase in OD increased the LR for infection substantially. A comparable increase in OD led to a much smaller increase in the LR for positive fecal culture. ODs higher than 0.35 made infection with the organism extremely likely.

For the same example of feline heartworm testing (see earlier in the chapter) the LR+ = (45/50)/(209/950) = 4.1, so that a cat with heartworm disease is four times as likely to have a positive test as a cat without heartworm disease. For LR– = (5/50)/(721/950) = 0.14, so a cat who tests negative is about 1/10th as likely to have heartworm disease as a cat without heartworm disease. These likelihood ratios will not change with changing prevalence.

If the pretest probability of disease or prevalence is estimated and a LR is known for a given test result (positive, negative or some range of results), then general guidelines for the effect of that particular likelihood ratio on the post-test probability of disease can be used. These guidelines are: LR = 0, no disease with that test result; LR = 0.1, lower probability of disease with that test result; LR = 1, no change in probability of disease with the test result; LR = 10, higher probability of disease after the test result; LR very high, disease is certain after test result. For LR between these values, the interpretations and impact on post-test probability of disease will be intermediate between the values.

Using More than One Test

What happens when we run a complete blood count and chemistry panel on an apparently health animal and get one result that is abnormal? Depending on the test, our

clinical experience may indicate that we can ignore that result. Numerically, this kind of result happens because "normal" is defined as the middle 95% of healthy animals' data. So by definition, 5% of healthy animals will have abnormal test results. Plus, if you perform 20 tests, the probability that one will test outside of normal is 0.95 * 0.95 * 0.95, or 20 times = 0.34. Or about one third of the time, the patient will have an abnormal test even the animal is healthy.

We often use many tests to make a decision about a diagnosis. When tests are formally combined, there are two approaches: testing in parallel and in series. In **parallel testing**, the patient is considered diseased if it is positive for any of the tests. Therefore, it is easy for a patient to come out positive and be considered diseased and difficult for a patient to be negative because it must be negative to all tests. This gives a more sensitive test and a high negative predictive value. Tests are usually interpreted this way when a quick assessment is needed to rule out some potentially serious problem; any positive animals then receive further work-up. This approach is also used for situations in which the animal needs to be considered healthy, such as a vaccination clinic or other situation in which a negative result must be correct.

The opposite approach is **testing in series**. A negative result on any test leads to a conclusion that the animal is free of the disease of interest. It is easy to be considered negative but the patient must be positive to

all tests to be considered diseased. So the specificity is high and the positive predictive value is high. It is used in settings in which false-negative results are not a problem and where ruling in a diagnosis is the main objective of the testing. This approach is often used for disease eradication programs in which positive animals are removed from the population and negative animals will continue to be tested.

Special Consideration for Applying the Results in the Practice Setting

Perhaps the most crucial question to ask is whether or not the results of the test will help the client or patient. Helpful tests most often provide a definitive diagnosis such that the best therapy can be instituted. They may also provide information about prognosis. However, sometimes there is very little choice about treatment regardless of the definitive diagnosis. This could occur when (1) there is only one available treatment; (2) there is only one affordable treatment; (3) there is only one treatment the owner can administer; or (4) there is only one treatment the patient will tolerate. In these situations, obtaining a definitive diagnosis may be an academic exercise unless the client really wants to know that diagnosis. Similarly, if the other reasons one might use a test are not important to the client or will not alter the management of the patient, it may not be appropriate to

use that test. The bottom line is: Will the patient be better off after the test than before?

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7

Making Decisions about Prognosis

A prognosis includes information about what could happen (given various events or choices) and how long it will take to happen. The relative costs of each intervention or choice may also be included. The concept of prognosis is closely allied with the natural history of the disease, which is the general progression of the disease beginning with the earliest cellular or biochemical changes. In some cases, prognosis is considered to be a subset of the natural history of the disease; that part of the disease

progression after diagnosis has been made until recovery, death, or some other important outcome.

In veterinary medicine, one often hears about prognoses that are "good" or "guarded," for example. The meaning of these terms varies widely and depends on the disease and outcome of interest, as well as on the listener's interpretation. A study at a university teaching hospital asked 62 large and small animal clinicians to describe how likely animals were to recover (from 0%, no animals recovered to 100%, all animals recovered) from an illness that was treated appropriately for each of a series of these qualitative terms.[1] Recovery was defined as absence of disease-related signs for at least 1 year with appropriate treatment or management. Of the 47 clinician who responded, the term "grave prognosis" was assigned percentages from 0 to 30% for recovery. For "fair prognosis." the percentages of patients that would recover was reported anywhere from 20% to100%. For a "good prognosis," 60% to 100% of animals would recover. This illustrates the variability in different clinicians' ideas of what constitutes a "good" prognosis. Imagine the confusion of the client! So, ideally, a real estimate of the percentage of patients that would recover or reach some other important outcome should be presented. This will assist in decision making about whether treatment should be instituted at all and, if so, what treatment will best satisfy the needs of the patient and client.

Quality of Information

Ideally, the prognosis should be determined using cohort studies. Specifically, an **inception cohort** should be assembled. This means that a representative group of patients are collected at a standard, usually early, point in their disease progression. These patients are then followed, and the outcomes of interest measured and described.

Follow-up in cohort studies is a key element. If the follow-up was not complete, too many patients may have been lost for important reasons (e.g., they did not tolerate the medication well, they died early in the course of treatment). A rule of thumb is that less than 5% losses to follow-up are likely not a problem, and greater than 20% may seriously compromise the validity of the results. The length of follow-up is also important. If it is too short, there may not be very much information about the outcomes of interest. The outcomes of interest must be clearly stated and defined, as should the methods to identify these outcomes. Ideally, the investigators should be blind to other patient characteristics that could effect outcome when measuring these events. However, if the outcomes are relatively objective and the tests used to determine them routinely applied to all patients (or clients), then blinding is much less of a problem.

Because the process by which each subject receives the particular exposures of interest is not random,

cohort studies may be subject to serious **bias**, that is, some systematic and important differences arise between the groups. An example might be: Could the healthier patients have been allotted to surgical rather than medical interventions? This means that determining whether the exposure groups were similar in regard to important factors that could affect the outcome *other than the exposure of interest* is especially critical in cohort (and other observational) studies. See Box 7-1 for some factors to consider.

Box 7-1. Common Potential Problem Areas that Could Affect the Comparability of the Different Exposure Groups in a Cohort Study

The type of service setting being compared

- Regional or national differences
- Referral versus primary care hospitals
- Teaching hospitals versus specialty private practice
- Single person versus multiple person practices

The type of treatment or exposure possible in that setting

- Referral center's high tech treatment options
- Specialist's expertise in performing certain procedures
- Access to experimental protocols or drugs

The time period of the treatment or exposure

- Emergency versus during routine clinic hours
- Management or level of care available changing with time period

In spite of some limitation in observational study designs, there are situations in which they are the most appropriate approach (or are the only type of study design available). Observational studies can be very useful in generating hypotheses to be tested more stringently in clinical trials. They may also be more realistic representations of real life and the actual benefits of particular treatments or exposures in the practice setting. Finally, if the outcomes are very rare or require a long time to occur, for practical reasons, only observational (and likely retrospective) studies will be able to evaluate them. It is just not feasible to enroll hundreds or thousands of subjects in a clinical trial and follow them for 10 years.

In veterinary medicine, for the previously mentioned reasons among others, prognostic studies often take the form of case series, in which a group of animals is identified (usually retrospectively from the medical records) because of some common characteristic such as diagnosis with a particular disease. Unfortunately, because these animals are often from referral hospitals and are likely to be relatively late in the course of disease, they are also preselected by the willingness of the owner to bring the animal to the referral hospital, the availability of a referral hospital, and the referring practitioner's expertise in that particular disease. Long-term information on outcome may be collected from the records on return visits or by telephone or mailed surveys, and losses to follow-up are often quite high. These losses are not always the fault of

the investigator or a result of the disease because, most commonly, the loss is due to the owner of the animal moving away without forwarding information. In addition, unless large numbers of animals are in the case series, there will not be enough data to divide them into subgroups and look for differences in prognosis that may be due to stage of disease, concurrent disorders, age, breed or sex, and other potentially important factors.

Published studies of prognosis are used by practitioners to try to predict the outcomes of other similar groups of animals. This means that it will be very helpful to know if the information has been validated in another group of patients. For example, if a model predicting survival from colic is produced from a data set, that model could be used in a new set of patients and shown to be fairly accurate in predicting their outcomes. When possible, the articles with validation often provide the best evidence for prognostic predictions. There is some published work that does this in the veterinary literature. One example is a study that evaluated data at admission and at surgery for dairy cows with right displacement of the abomasum (RDA) or abomasal volvulus (RAV).[2] The cows were included if they were seen at the New York State College of Veterinary Medicine between 1980 and 1987 with a final diagnosis of RDA or RAV. The final outcomes of interest were classified into productive (eating and milking normally), salvaged (alert but off feed and milk), and terminal (died or

were euthanized during hospitalization). Three variables at admission were found to be good predictors in a statistical model of the three outcomes: heart rate, base excess, and plasma chloride concentration. Five variables from surgery were good predictors of the three outcomes: heart rate, base excess, diagnosis, method of decompression, and appearance of abomasal serosa. The data were displayed such that a cow that presented for RDA could have the data at admission entered into the equation and the probabilities for productive, salvaged, and terminal outcomes calculated. This information could then be used to decide if it would be worthwhile to pursue surgery given the value of the cow. This study's main weakness was that the data were obtained retrospectively so that 123 of the original 458 cows had missing data and were excluded from the study. The authors did provide this information, and the breakdown of outcomes for the original and complete-data cows. The endpoints were intended to be practical for a dairy farmer. but the actual on-farm outcome of each cow was not obtained. Box 7-2 provides a list of questions for studies on prognosis. The more "yes" answers, the better the study.

Results for Studies of Prognosis

The quantification of prognosis often includes measures of incidence and at times, comparison of incidence

Box 7-2. Key Elements of Prognostic Studies

1. Was a clearly defined sample of patients identified?
2. Were the patients at a relatively similar point in the disease process?
3. Was the follow-up complete (>80%) and of sufficient length to assess the outcomes?
4. Did the outcomes reported include the relevant endpoints measured as objectively as possible?
5. Were other important prognostic factors accounted for by statistical analysis or separation into logical subgroups?

between subgroups. Therefore, cumulative incidence, incidence density, relative risk, and risk differences may all be reported. Keep in mind that the size of the group studied affects the precision of these outcome measurements and, therefore, their usefulness. For instance, if 30 animals are included and none have the outcome of interest at the end of the study, the true frequency of the outcome could still be as high as 10%. For 10 animals, the true frequency could be as high as 26% and for five, as high as 45%. Similarly, if all 30 of the animals have the outcome of interest, the true frequency in the population could be as low as 90%, for 10 animals as low as 74%, and so on.

Prognosis may also be expressed in terms of **survival rates** (such as 1-year survival percentage), **case fatality rate** (number of deaths divided by the number of ani-

mals with the disease), or **median survival time** (the length of time the patients are still alive), or by using survival curves that graphically display the percentage of animals surviving at each given time.

Formal survival analysis measures the time until the outcome (death or other event) and accounts for animals that have not yet have the outcome occur during the course of the study or that are lost to follow-up. Life table analysis and Kaplan-Meier analysis may be used in this case. To include information on other potentially important prognostic factors, a Cox proportional hazards model may be used. Like other types of survival analysis, this technique evaluates time to the outcome; the advantage is that it simultaneously adjusts for the affects of other factors. A relative risk can be calculated from the model, and predicted survival for other similar patients can be calculated using an equation derived from the model. For example, in a study on survival after radioactive iodine treatment for hyperthyroidism in cats, age at diagnosis and sex (male versus female) were found to be the only important predictors of survival for cats following treatment and discharge from the hospital.[3] Female cats were 0.68 times more likely to die than male cats (so female cats were 1/0.68 or 1.4 times more likely to survive than male cats), and increasing age at diagnosis increased risk of dying (by 1.2 times per year of increasing age). The Cox proportional hazards model was used to calculate predicted survival for different age

and sex combinations, and the results were tabulated in the article for easy application to a new feline patient. Although the results of the study were not validated in a new set of cats and the study was performed in a referral institution, these results could prove useful in some settings for clients with hyperthyroid cats who are trying to decide if it would be worthwhile to go through the trouble, stress, and expense of radioactive iodine treatment in their older cats.

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8

Making Decisions about Causation or Etiology

Questions about **causation** or etiology revolve around decisions as to whether some characteristic, disease, treatment, or event directly leads to a particular endpoint. This means that some exposure increases (or in some cases, decreases) the likelihood of a particular outcome. In the situation in which an exposure results in a decrease in the outcome, terms such as *prevention* or *protective* are commonly used. Similarly, assessing the possibility of a treatment causing an adverse effect

can be thought of as determining causation. Causes, causation, and etiology are used interchangeably in this chapter. Evaluating evidence about all of these situations is done in the same way.

The ideas behind proving that some exposure causes some outcome are complex. Causation is not proven based on a statistical test alone and it would be exceedingly rare to be based on a single study. Veterinarians must use all available information and decide in their own minds whether some exposure really causes some outcome. As an example, the profession is currently in the middle stages of understanding the role of vaccination or injection and the occurrence of sarcomas at the injection site in cats. Although many veterinarians believe that there is clearly a causal relationship of some sort between some injections and sarcomas, many details are still vague and controversial. The role of the specific vaccine, adjuvant, or injection technique, as well as the age, breed, and immune status of the cat, are still under investigation.

Quality of Information

In looking at clinical research and epidemiologic studies, once again, **randomized controlled clinical trials** provide the strongest evidence that an exposure caused a disease or event. However, clinical trials are even less commonly performed for causation than for other types of clinical questions, often for practical or ethical rea-

sons because the exposure of interest is often not readily controlled or assigned. Some exposures such as breed or sex obviously cannot be assigned. Often, management factors, such as feeding, exercise patterns, and housing, cannot be readily modified even for short periods of time.

Cohort studies provide the next best evidence and are more often used because the exposure can be measured, and the exposed and unexposed groups followed for the outcome of interest. For example, obesity in horses has been proposed as a potential cause of laminitis. A clinical trial in which horses were assigned to regimens to make one group obese and keep another at optimal body condition under real world conditions is not practical for many reasons. However, identifying a group of obese horses and a group of nonobese horses, and measuring the incidence of laminitis in each group over time might be possible. Cohort studies are limited, compared with randomized clinical trials, by the lack of random assignment of exposure, increased potential for confounding, importance of assessing exposure and outcome similarly in both exposure groups, and often large numbers of animals needed for relatively uncommon outcomes to occur. In the case of laminitis in horses, all horses would have to be free of laminitis at the beginning of the study. This can be difficult to ascertain even with radiographs. Clear definitions of obese and nonobese would have to be developed and applied

consistently for all horses. Other potential predisposing factors for laminitis, such as feeding, housing, breed, and age, would have to be measured and accounted for. Owners would have to be knowledgeable about early signs of laminitis. Owners of the obese horses might be more inclined to call their veterinarian for a subtle lameness compared with owners of nonobese horses, because they might already know about the suggested link between obesity and laminitis, biasing the assessment of the outcome. To have enough horses develop laminitis for the study outcome would require a very large number of animals and a prolonged follow-up time, especially because good estimates of the frequency of laminitis are not available.

Case-control studies provide weaker evidence of causation than cohort studies but are often more practical in veterinary medicine. They are still the best choice for very rare or delayed outcomes or adverse effects that take extremely long periods of time to develop. However, because exposure is often measured using what people can remember or what is written in a medical record, it may not be unbiased or correct. Horses with newly diagnosed laminitis and horses without laminitis could be included in the study and their level of obesity before the onset of the disease measured. Fewer horses would be needed, and they would not need to be followed across time for many years. The difficulty here is determining obesity before disease onset and separat-

ing out horses that are obese because of previous laminitis and lack of work from horses without a history of laminitis. If the present owner has owned the horse for much of its life, this information may be available. But a recent owner or a horse with many owners will have an unknown health history.

Cross-sectional studies may be used as an initial quick and dirty design for causation. This design provides the weakest evidence, particularly if no attempts were made to account for potential confounding factors. This study design is often used because of how quickly and inexpensively it can be completed. Because exposure and outcome are assessed at the same time, the time course of events may be unclear. For the laminitis example, an association would likely be found for obese horses to be more likely to have laminitis than nonbese horses. But it would be impossible to determine if the obesity caused the laminitis (or helped cause it) or if the laminitis led to a decrease in exercise or work and therefore resulted in obesity.

Case series may be published that simply report that some exposure seems to be linked to some outcome, particularly in the situation of adverse treatment effects. These studies do provide a heads up that there could be a problem, like diazepam (Valium) and liver problems in cats. However, these studies can and often will be overinterpreted. They are really just the first step in determining if an exposure causes an effect. For instance,

embedded in a case-control study of sex, hair length, and breed as risk factors for heartworm disease in cats, indoor-outdoor status (as reported by owners of 48 of 50 cats) was presented.[1] The authors concluded that because 13 positive cats were reported to be indoor only, indoor status was only partially protective from heartworm disease. Because no comparison group was used and no estimate of time spent outside for indoor-outdoor cats was available, no discussion of the size of the risk for indoor only cats was possible. Based on this and one additional study (of three indoor cats out of nine positives),[2] the conclusion was that indoor cats were also at risk for heartworm disease, and veterinarians in the south are often recommending heartworm prevention for indoor-only cats. Box 8-1 lists the important components of studies on causation. The more "yes" answers, the better the study.

Results for Studies of Causation

There are a number of common sense criteria to apply when thinking about, measuring and documenting causation. These are usually based on Hill's early work on smoking and lung cancer.[3] More recent modifications by Evans include some useful points and are discussed by Thrusfield. Not all of these criteria may be fulfilled, and some may be more important for certain situations than others. Consider the list in Box 8-2 as guidelines only except for point 1.

Box 8-1 Key Elements for Studies about Causation

1. Was the study design the best that could be done from a practical perspective?
2. Were the different exposure groups as similar as possible in important ways or, failing that, were confounders measured and accounted for in the analysis?
3. Were exposure and outcome determinations done the same way in all groups (blindly, if possible)?
4. Was the follow-up long and complete enough (in clinical trials, cohort studies) for the outcome of interest to occur?
5. Did the exposure precede the outcome?
6. Was the association between exposure and outcome statistically significant?
7. Was the association between exposure and outcome clinically significant?

To quantify risk, an increase or decrease in the relative risk (RR) or odds ratio (OR) should be found if causation is to be plausible. The RR and OR must be statistically significantly different from one (which means that there is no difference in risk between the groups). A *P* value will tell this. A better option is a 95% confidence interval. If the confidence interval for the RR or OR includes one then there is not a significant change in risk between groups. How big is a big enough change in risk? For RR in a very good clinical trial, any significant RR is likely big enough. For a

Box 8-2. Guidelines for Making Decisions about Causation or Etiology

1. The exposure must precede the disease.
2. The outcome should occur more commonly in those that are exposed than in those that are not.
3. The severity of disease should vary with the extent or intensity of exposure.
4. Removing the exposure should decrease the frequency of the outcome. For temporary outcomes like adverse drug effects, the adverse effect should go away when the drug is discontinued and then recur when the drug is reintroduced.
5. There should be a reasonably strong (big) effect of the exposure on the outcome as measured by the relative risk or odds ratio. This effect should be clinically important (big enough to make a difference to a patient or client) and statistically significant.
6. The cause and effect should make sense given what is currently known about the disease.
7. Laboratory experiments should be consistent with epidemiologic data.

cohort study, a RR of three is a good guideline. For an OR, because of the extra opportunities for bias from a case-control study, four might be a reasonable OR to believe (see Thursfield). ORs are interpreted in the same way as RRs.

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9

Sources of Information on Zoonoses

Laura E.Robinson

Knowledge and awareness of zoonotic diseases is increasingly important for today's veterinarian. Discussing issues such as emerging and reemerging diseases, antibiotic-resistant pathogens, pet ownership by immune-compromised persons, ownership of exotic wild pets and bioterrorism preparedness requires an understanding of the variety and scope of diseases that can be transmitted from animals to people. With the proliferation of

web sites and internet discussion groups specializing in veterinary medicine and public health, finding current information about zoonotic disease risks can be as straightforward as a literature search using PubMed, posing a question to specialists through e-mail, or using an internet search engine such as Google or Lycos.

State health departments and agricultural agencies can also be important sources of information about enzootic diseases in your practice area. Some states may even require that veterinarians report diseases of public health significance. Historically, rabies has been one of the few animal diseases required to be reported to the local or state health department. However, with the introduction of West Nile virus and the threat of bioterrorism, many public health officials are relying on the veterinary community to provide reports of unusual disease syndromes, uncommon diseases, or outbreaks of high morbidity or mortality in animal populations.

Disease-reporting requirements for veterinarians vary by state. In general, livestock diseases of economic importance are regulated by the U.S. Department of Agriculture's Animal and Plant Health Inspection Service and the State Veterinarian. Information on livestock disease regulatory authorities can be found at http://www.aphis.usda.gov/vs/area_offices.htm. Animal diseases of public health importance may be reportable to the state or local health department, and

contacting your State Health Department directly is the best way to determine your reporting responsibilities. Another important resource for veterinarians concerned about zoonoses is the State Public Health Veterinarian, although not all states have this position. The Association of State and Territorial Health Officials (ASTHO) web site: http://www.astho.org/state.html, has links to each state's health department web site. A listing of the notifiable human diseases, which can include zoonoses, for each state is listed at http://www.cste.org/reporting%20requirements.htm, the Council of State and Territorial Epidemiologists' web site.

Prevention of Disease Transmission

The key to preventing transmission of zoonoses is recognizing that a particular illness may be caused by a zoonotic organism. Zoonoses should be included in the differential diagnoses for the various disease syndromes listed in Chapter 10, particularly those that include diarrhea. If a zoonotic disease is suspected, the diagnosis should be confirmed through laboratory testing, and treatment should include other susceptible animals in the household to prevent reinfection from healthy carriers. Owner education about the sources of disease and methods of transmission among animals and to people is especially important. If an owner or family member is

exhibiting symptoms that could indicate infection, he or she should be urged to see their physician and indicate that their pet has been diagnosed with a zoonotic disease. Veterinarians should also be prepared to consult with physicians regarding the possibility and routes of zoonotic disease transmission. Veterinarians should contact their local health department or State Public Health Veterinarian if unusual numbers or patterns of zoonotic diseases are occurring, or if they have concerns about a common environmental source of infection that may be a public health hazard.

10

North American Zoonoses by Species and Major Organ System Affected

Laura E.Robinson

Tables 10-1 to 10-5 list zoonoses of public health importance or those that may cause concern to owners of affected pets. For brevity, food-borne and vector-borne zoonoses are not included if they are not generally associated with situations a veterinarian would encounter in a clinical practice.

Table 10-1. North American Zoonoses of Dogs and Cats of Significance in Private Practice

Zoonosis	Organism	Transmission	Prevention
Brucellosis	*Brucella canis*	Contact of placental fluids, aborted tissues, urine or reproductive fluids with mucous membranes or open cuts	Diagnose and treat infected dogs; limit contact with reproductive fluids and tissues from potentially infected dogs
Cat-scratch disease, bartonellosis	*Bartonella henselae, B. quintana*	Scratches and bites from cats and possibly dogs	Handle pets gently to reduce the possibility of scratches; clean and disinfect bites and scratches immediately; practice strict flea control
Chagas' disease, American trypanosomiasis	*Trypanosoma cruzi*	Potentially through contamination of open wounds with blood or tissues of infected dogs	Limit contact with blood from infected dogs, which may include spaying infected bitches; handle blood specimens carefully; exercise care during necropsy of potentially infected dogs
Conjunctivitis	*Chlamydia psittaci*	Potentially through contact with conjunctival exudates of infected cats	Wash hands thoroughly after medicating cats with conjunctivitis
Diarrhea	*Salmonella* spp., *Campylobacter* spp., *Yersinia* spp., *Giardia* spp., *Cryptosporidium parvum,* other organisms	Fecal-oral	Wash hands thoroughly after contact with pet feces; diagnose and treat pets with diarrhea
Echinococcosis	*Echinococcus granulosus, E. multilocularis*	Fecal-oral	Wash hands thoroughly after contact with pet feces; do not allow pets to eat wild rodents;

			perform regular fecal exams on outdoor and hunting pets
Larval migrans	*Toxocara canis, T. cati, Ancylostoma braziliense, A. caninum*	Fecal-oral (*Toxocara* spp.); penetration of skin by larvae (*Ancylostoma* spp.)	Examine and treat pets for intestinal parasites regularly, especially if they will be in contact with children; treat all newly acquired puppies and kittens; dispose of animal feces properly
Leishmaniasis	*Leishmania donovani*	Contact of open wounds with material from skin lesions; bites from infected sandflies	Wear latex gloves when handling animals suspected of having cutaneous leishmaniasis; avoid needlestick injuries when treating infected dogs or cats; exercise care during necropsy of potentially infected dogs
Leptospirosis	*Leptospira interrogans*	Contact of mucous membranes or broken skin with infected urine	Diagnose and treat infected dogs; vaccinate dogs in endemic areas; avoid splashing and aerosolization of urine when cleaning dog kennels; clean and disinfect areas contaminated with infected urine
Plague	*Yersinia pestis*	Bites from infected fleas; airborne droplets from cats with pneumonic plague; contact of mucous membranes or broken skin with saliva, tissues, or purulent material from infected animal	Practice strict flea control; do not allow pets in plague-endemic areas to eat wild rodents; isolate cats suspected of having plague and wear personal protective equipment to prevent airborne spread; disinfect or dispose of all surfaces or materials in contact with purulent materials and respiratory fluids

Continued

Table 10-1. North American Zoonoses of Dogs and Cats of Significance in Private Practice—cont'd

Q fever	*Coxiella burnetii*	Aerosolized birth fluids from parturient cats; tickborne transmission from infected dogs	Limit pet's contact with infected livestock and their tissues; thoroughly clean and disinfect surfaces and materials contaminated by birth fluids; practice strict tick control
Rabies	Rabies virus	Bites, contact of open wounds or mucous membranes with infected saliva or nervous tissue	Immediately wash bites and scratches with soap and water; report bite incidents to local health officials; vaccinate dogs and cats
Ringworm	*Microsporum* spp., *Trichophyton* spp.	Contact with infected animal or contaminated materials (brushes, etc.)	Limit contact with animals with patchy hair loss or typical circular lesions
Scabies	*Sarcoptes scabiei*	Contact with infested animal or contaminated materials (e.g., bedding and clothing)	Limit contact with pruritic animals; treat animals and clean environment, including bedding, simultaneously
Sporotrichosis	*Sporothrix schenckii*	Direct contact with cutaneous lesions and suppurative exudates of infected cats	Wear gloves and thoroughly disinfect hands and arms after handling cats suspected of having sporotrichosis
Toxoplasmosis	*Toxoplasma gondii*	Ingestion of undercooked beef, pork, or mutton; ingestion of sporulated oocysts from environments contaminated by cat feces (gardens, infrequently cleaned litter boxes, surfaces contaminated with cat feces)	Dispose of cat feces daily; clean and disinfect litter box at least weekly; wash hands after gardening, collecting cat feces, and cleaning litter box; wear soil-impervious gloves while gardening; do not allow pet cats to eat wild birds or

			rodents; limit cats' access to gardens and children's sandboxes and playgrounds
Tularemia	*Francisella tularensis*	Bites; contact of mucous membranes or open wounds with infected saliva or tissues; tickborne transmission from infected dogs	Do not allow pets to eat wild rabbits or rodents; practice strict tick control; wear gloves and a face shield when handling infected pets
Wound infections	*Pasteurella multocida, P. haemolytica, Capnocytophaga canimorsus, C. cynodegmi*	Bites, scratches	Handle pets gently to reduce the possibility of scratches; immediately clean and disinfect bites and scratches; seek medical attention if wound develops signs of infection; prophylactic antibiotics may be prescribed in some case

Table 10-2. North American Zoonoses of Birds of Significance in Private Practice

Zoonosis	Organism	Transmission	Prevention
Dermatitis	Straw itch mite, *Dermanyssus gallinae, Ornithonyssus* spp.	Contact with infested bird, bedding, or dander	Examine and treat for mites if feather loss or itching is noted; do not allow caged birds to have contact with wild birds
Diarrhea	*Salmonella* spp, *Campylobacter jejuni, Yersinia pseudotuberculosis*, *Cryptosporidium parvum,* other organisms	Ingestion of fecal material	Wash hands after handling birds and cleaning cages; do not clean cages in areas used for preparation or consumption of food; use a detergent and disinfectant when cleaning cages.
Histoplasmosis	*Histoplasma capsulatum*	Inhalation of fungus growing in accumulated droppings	Do not allow droppings to accumulate in bird cages, chicken pens, or outdoor bird roosts; thoroughly clean and disinfect surfaces after removing droppings
Psittacosis	*Chlamydia psittaci*	Inhalation of organism in dust from feces, secretions, or feathers	Treat birds before allowing to visit or live in classrooms; clean cages frequently to avoid accumulation of potentially infectious materials
Ringworm	*Trichophyton gallinae*	contact with infected bird or contaminated materials	limit contact with birds with patchy feather loss or feather damage

Table 10-3. North American Zoonoses of Rodents of Significance in Private Practice

Zoonosis	Organism	Transmission	Prevention
Dermatitis	*Sarcoptes scrabiei, Ornithonyssus bacoti*	Contact with infested rodents, bedding, or cages	Examine and treat rodents for mites; eliminate contact with wild rodents.
Diarrhea	*Salmonella* spp, *Campylobacter* spp, *E. coli, Yersinia* spp., *Giardia* spp., *Cryptosporidium parvum,* other organisms	Fecal-oral	Wash hands after handling animal and cleaning cages; do not clean cage in areas used for food preparation or consumption; perform antimicrobial susceptibility testing of isolates
Flea-borne typhus	*Rickettsia typhi, R. felis*	Contamination of skin wounds with infected flea feces	Practice strict flea control; exclude wild rodents and opossums from premises
Hantavirus pulmonary syndrome	Hantaviruses	Inhalation of dried feces, saliva or urine	Do not allow contact between wild and captive rodents; do not keep wild-caught rodents as pets; store animal foods in rodent-proof containers
Lymphocytic choriomeningitis (LCM)	Arenavirus	Inhalation, ingestion or contact with the urine, saliva or feces of infected animals	Obtain pet from LCM-free colony; do not allow contact between captive and wild rodents, especially mice; store animal foods in rodent-proof containers

Continued

Table 10-3. North American Zoonoses of Rodents of Significance in Private Practice—cont'd

Zoonosis	Organism	Transmission	Prevention
Rat-bite fever	*Streptobacillus moniliformis, Spirillum minus*	Bites from rodents (primarily rats), ingestion of fluids contaminated with rodent urine, saliva or nasolacrimal secretions.	Handle animals humanely to avoid provoking a bite
Ringworm	*Microsporum* spp., *Trichophyton* spp.	Contact with infected animal or contaminated materials (e.g., bedding)	Limit contact with animals with patchy hair loss or typical circular lesions
Tapeworm infection	Dwarf tapeworm (*Hymenolepis nana*), rat tapeworm (*H. diminuta*)	Fecal-oral, contamination of environment with ova in feces, consumption of larvae-infected insects	Wash hands after handling animal and cleaning cages; treat mice, rats and hamsters with anthelmintics; feed only commercially prepared food which is not infested with insects

Table 10-4. North American Zoonoses of Reptiles, Exotics, and Wildlife of Significance in Private Practice

Zoonosis	Organism	Transmission	Prevention
Diarrhea	*Campylobacter* spp, *E. coli, Yersinia* spp., *Giardia* spp., *Cryptosporidium parvum,* other organisms	Fecal-oral	Wash hands after handling animal and cleaning cages; do not clean cage in areas used for food preparation or consumption; perform antimicrobial susceptibility testing of isolates
Granuloma	*Mycobacterium marinum*	Contact of open wounds with aquarium water; handling infected fish	Do not allow persons with skin wounds on hands or arms to clean aquarium; clean aquarium regularly; wear gloves when handling fish
Herpes B	*Herpesvirus simiae*	bites and contamination of broken skin or mucous membranes with saliva or body fluids from *Macaque* monkeys	Immediately wash all bites, scratches, and mucous membranes that have been in contact with body fluids from *Macaque* monkeys; evaluate the bite victim and the biting monkey for infection
Larval migrans	*Baylisascaris procyonis*	Fecal-oral	Do not keep raccoons as pets; wash hands immediately after contact with raccoon feces or materials contaminated by raccoon feces
Necrotizing cellulitis, septicemia	*Vibrio vulnificus*	Contact of open wounds with aquarium water; penetrating wounds from fish spines	Avoid handling fish directly; do not allow persons with skin wounds on hands or arms to clean aquarium

Continued

Table 10-4. North American Zoonoses of Reptiles, Exotics, and Wildlife of Significance in Private Practice—cont'd

Plague	*Yersinia pestis*	Flea bites; contact with tissues from infected rodents	Do not obtain pet prairie dogs, squirrels, or other rodents from plague endemic areas; do not keep wild rodents as pets; practice strict flea control
Rabies	Rabies virus	bites, contact of open wounds or mucous membranes with infected saliva or nervous tissue	Do not keep high-risk species such as raccoons, bats, skunks, foxes, or coyotes as pets; immediately wash bites or scratches with soap and water; report bite incidents to local health officials
Ringworm	*Microsporum* spp., *Trichophyton* spp.	Contact with infected animal or contaminated materials (e.g., bedding)	Limit contact with animals with patchy hair loss or typical circular lesions
Salmonellosis	*Salmonella* spp.	Fecal-oral	Wash hands after handling reptiles and cleaning animal's cage or terrarium; do not clean cage or terrarium in food preparation area; do not allow animals in areas where food is prepared or consumed
Shigellosis, dysentery	*Shigella* spp.	Fecal-oral	Diagnose and treat nonhuman primates exhibiting bloody diarrhea; wash hands and surfaces after contact with feces
Tuberculosis	*Mycobacterium tuberculosis, M. bovis*	Droplets in aerosols	Examine and screen pet nonhuman primates and brushtail possums for infection; protect nonhuman primates from people with infectious tuberculosis

Table 10-5. North American Zoonoses of Livestock and Horses of Significance in Private Practice

Zoonosis	Organism	Transmission	Prevention
Anthrax	*Bacillus anthracis*	Contact of broken skin with spores; inhalation or ingestion of spores	Do not perform a necropsy on animals suspected of dying of anthrax; incinerate carcasses or bury deeply with quick lime; vaccinate livestock in endemic areas; do not handle hides, wool, or hair of animals that have died of anthrax
Brucellosis	*Brucella abortus, B. melitensis, B. suis*	Ingestion of unpasteurized milk or milk products; contact of birth fluids with mucous membranes; inhalation of aerosols from birth fluids	Vaccinate or test animals as required by law; pasteurize milk before consumption and processing; wear gloves and eye protection when assisting with parturition; test animals which abort or have stillbirths
Diarrhea	*E. coli, Campylobacter jejuni, Salmonella* spp., *Cryptosporidium parvum*	Fecal-oral	Wash hands after handling animal and cleaning pen; identify and treat animals with diarrhea
Leptospirosis	*Leptospira interrogans*	Contact of abraded skin or mucous membranes with urine; ingestion of urine-contaminated materials; inhalation of infected fluids	Vaccinate animals to prevent disease; wash hands after handling animal and cleaning pen; wear eye protection if using water spray to clean pen; eliminate rodents from animal's living quarters; store feed in rodent-proof containers; ensure proper drainage and disposal of urine from pens and pastures

Continued

Table 10-5. North American Zoonoses of Livestock and Horses of Significance in Private Practice—cont'd

Zoonosis	Organism	Transmission	Prevention
Orf (Contagious ecthyma)	Orf virus	Skin contact with goat or sheep pox lesions	Obtain sheep and goats from a reputable source; restrict handling of sheep and goats with lesions; use gloves and wash hands after handling infected animals
Q fever	*Coxiella burnetii*	Contact of birth fluids with mucous membranes; inhalation of aerosols from birth fluids; direct contact with infected animals, bedding, wool; ingestion of unpasteurized milk	Test sheep, goats and cattle; obtain animals from a reputable source; wear gloves and eye protection while assisting with parturition; test animals that abort or have stillbirths; pasteurize milk before consumption and processing
Rabies	Rabies virus	Bites, contact of open wounds or mucous membranes with infected saliva or nervous tissue	Immediately wash bites and scratches with soap and water; report bite incidents to local health officials; vaccinate livestock and horses that are handled regularly or come in contact with large numbers of people
Ringworm	*Microsporum* spp., *Trichophyton* spp.	Contact with infected animal or contaminated materials (e.g., brushes, blankets)	Limit contact with animals with patchy hair loss or typical circular lesions
Tuberculosis	*Mycobacterium bovis*	Ingestion of unpasteurized milk or dairy products; airborne	Test cattle in accordance with state and federal guidelines; consume only pasteurized milk products; limit contact of livestock with wildlife including deer and elk

Table 10-6. Common North American Zoonoses by Presenting Major Organ System

Organ System	Presenting Signs	Animal Hosts	Zoonosis	Organism
Cardiovascular	Acute death, hemorrhage from body orifices	Herbivores (livestock and wildlife), swine	Anthrax	*Bacillus anthracis*
Cardiovascular	Acute death, generalized lymphadenopathy, myocarditis, dilatative cardiomyopathy	Dogs	Chagas' disease, American trypanosomiasis	*Trypanosoma cruzi*
Gastrointestinal	Diarrhea	All vertebrates	Diarrhea	*Salmonella* spp., *E. coli, Campylobacter* spp., *Yersinia* spp., *Giardia* spp., *Cryptosporidium parvum,* other organisms
Gastrointestinal	Mild diarrhea, rough coat, unthriftiness	Dogs, cats	Echinococcosis	*Echinococcus granulosus, E. multilocularis*
Gastrointestinal	Mild diarrhea, rough coat, unthriftiness	Dogs, cats	Larval migrans	*Toxocara canis, T. cati, Ancylostoma braziliense, A. caninum*
Gastrointestinal	Diarrhea, sometimes with blood and mucous	Nonhuman primates	Shigellosis, dysentery	*Shigella* spp.
Renal	Fever, anorexia, vomiting, renal insufficiency or failure, hematuria, icterus	Wild and domestic animals	Leptospirosis	*Leptospira interrogans*

Continued

Table 10-6. Common North American Zoonoses by Presenting Major Organ System—cont'd

Organ System	Presenting Signs	Animal Hosts	Zoonosis	Organism
Integumentary	Feather loss, feather picking	Birds	Dermatitis	Straw itch mite, *Dermanyssus gallinae,* Ornithonyssus *spp.*
Integumentary	Pruritus, dermatitis	Rodents	Dermatitis	*Sarcoptes scrabiei, Ornithonyssus bacoti*
Integumentary	Hyperkeratosis, nodular lesions, weight loss, muscle atrophy	Dogs, cats	Leishmaniasis	*Leishmania donovani*
Integumentary	Encrusted lesions on lips and oral mucosa	Sheep, goats	Orf (contagious ecthyma)	Orf virus
Integumentary	Circular hair loss	Domestic and wild mammals	Ringworm	*Microsporum* spp., *Trichophyton* spp.
Integumentary	Pruritus, mange, crusty dermatitis	Domestic and wild mammals	Scabies	*Sarcoptes scabiei*
Integumentary	Cutaneous nodules, ulcers, and draining tracts	Cats	Sporotrichosis	*Sporothrix schenckii*
Integumentary	Fever, mucopurulent ocular and nasal discharge, pustular or papular dermatitis, lymphadenopathy	Dogs, cats	Tularemia	*Francisella tularensis*

Lymphatic	Fever and lymphadenopathy in dogs and cats; draining abscesses and pneumonia in cats; acute death in rodents	Dogs, cats, rodents	Plague	*Yersinia pestis*
Lymphatic/respiratory	Fever, lymphadenopathy; pulmonary tuberculosis in nonhuman primates	Cattle, exotics, wildlife	Tuberculosis	*Mycobacterium tuberculosis, M. bovis*
Neurologic	Ataxia, aggression, change in behavior, unexplained paralysis, seizures, cranial nerve paralysis, unexplained death	Mammals and marsupials	Rabies	Rabies virus
Reproductive	Stillbirths, abortions, weak neonates	Cattle, sheep, goats, cats	Q fever	*Coxiella burnetii*
Reproductive	Females: infertility, abortions, weak neonates Males: infertility, epididymitis, prostatitis	dogs, livestock, equine	Brucellosis	*Brucella canis, B. abortus, B. melitensis, B. suis*
Respiratory	Conjunctivitis, upper respiratory disease	Cats	Conjunctivitis	*Chlamydia psittaci*
Respiratory	Depression, dyspnea, ruffled feathers, diarrhea	Birds	Psittacosis	*Chlamydia psittaci*

Many zoonotic organisms comprise the normal oral, gastrointestinal, or dermal flora of animals or do not cause overt disease unless there is an overwhelming infection or infestation. Table 10-6 lists those zoonoses associated with clinical illness in animals by major presenting organ system.

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11

Handling Outbreaks of Disease

Laura E.Robinson

Is an Outbreak Occurring?

The definition of an outbreak or epidemic is the occurrence of a greater number of cases of a particular disease than is expected or normal. There is no set number that can be used universally to define the threshold for "normal" versus "an outbreak." In some instances, an outbreak can occur if there is one case of an unusual

disease, particularly if it is a foreign animal disease in livestock or a more common disease affecting an unusual population or species. Cases occurring in an unusual geographic location or at an unusual time of year may also indicate an outbreak. In each circumstance, it is important to verify the diagnosis, understand the natural epidemiology of the disease in question, and know which diseases are endemic where exposure occurred.

Demonstrating an Outbreak has Occurred

Several steps are necessary to determine whether an outbreak has occurred. First, define the time period of interest, and the geographic area to be evaluated. The area may be the catchment area for a veterinary hospital or clinic, the municipality or county, or the whole state. The primary limitation is being able to obtain disease incidence data for the animals in that area for the time periods both before and during the suspected outbreak. The number of cases of a particular disease that occurred before the suspected outbreak is used to determine the "normal" or background incidence of that disease in that area. Within a clinic setting, these data may be found in patient records, onsite laboratory test logs, or laboratory reports. Having a computerized record keeping system in a database format that is searchable by disease diagnosis (such as ICD-9 code), species, sex, and age are ideal for determining the epidemiology of a dis-

ease in the clinic's patient base. Sources of disease incidence data for larger geographic areas might include colleagues in the local veterinary association, the state Veterinarian (in cases of a reportable livestock disease), specialty veterinary organizations, or the state veterinary diagnostic laboratory. Published studies may include information on the expected disease incidence in a particular population or provide a point of contact for further inquiry. These studies may also provide references to veterinary colleges or research institutions specializing in the disease of interest.

General Approach to Outbreak Investigation and Resolution

After determining the background incidence of a disease you can use this information to evaluate whether the number of cases occurring during the suspected outbreak is actually greater than expected. It is important to verify the diagnosis on each case especially if clinical signs are similar to other disease syndromes. Information to consider in the case definition includes the clinical signs, duration, and progression of the disease. Depending on what laboratory tests are available and the completeness of data collected for each suspected case, a case definition can be created to define further the clinical picture and identify additional cases. The concepts of sensitivity and specificity can also be applied

to the case definition to refine the case finding process. For example, if the disease is life threatening without early intervention, a broader, or highly sensitive case definition might be more appropriate. In other words, a high negative predictive value is needed so that a negative result is likely correct. This means that very few animals with disease will incorrectly be labeled as disease free (low false-negative rate). The trade off is an increased number of false-positive animals to sort out from the truly diseased animals. In contrast, a disease presenting with more common clinical signs and requiring laboratory testing for definitive diagnosis may indicate the need for a case definition with higher specificity. This would provide few false-positive results and a better positive predictive value. In this situation, there would be more false-negative animals that would require additional testing. After identifying additional suspect cases using the case definition, it is important to use confirmatory tests to diagnose the illness definitively. Otherwise it will be difficult to evaluate the effectiveness of treatment and control measures.

In a clinical setting, diagnosis followed by treatment is the final process in resolving an animal's illness. However during an outbreak, further epidemiologic evaluation and population-based interventions are often necessary after the initial diagnosis and treatment of individual affected animals (Box 11-1). The next step is to describe the characteristics of the affected animals

Box 11-1. General Steps for Investigating an Outbreak

1. Describe the time, location and signalment of the affected animals.
2. Establish a case definition that clearly diagnoses affected animals.
3. Determine the normal level of the disease and compare with the present level of disease to confirm that an outbreak has occurred or is occurring.
4. Identify affected animals and treat, isolate, or cull as appropriate.
5. Use epidemiologic studies to test hypotheses about the identity of the disease, its source, and its predisposing factors. This includes comparing animals with and without disease (case-control studies) or animals with or without the hypothesized exposure (cohort study).
6. Develop treatment and prevention protocols.
7. Monitor and evaluate the control and prevention of the disease.
8. Report the findings in written and oral formats.

and determine if there are important differences compared with the general population. Data collected at this stage include signalment of the animals, as well as location and time course of event. This descriptive epidemiology can be used in conjunction with the disease's pathogenesis to identify the population at risk and develop hypotheses regarding the identity and source of exposure. Environmental and laboratory testing may be

incorporated at this time, as well as later in the investigation. Epidemiologic tools such as case-control studies and cohort studies can then be used to evaluate these hypotheses and refine them as needed. This process of testing hypotheses using epidemiologic studies may need to be done more than once to determine definitively the source of the outbreak. These studies allow the veterinarian to evaluate risk factors for animals that get the disease and develop logical treatment and control schemes. Finally, preventive measures to reduce exposure in the population at risk reduce the incidence of the disease, whereas identification and treatment of existing cases reduce the prevalence of the disease, thus controlling the outbreak. As with the hypothesis-generating process, continued monitoring and evaluation of the prevention and control measures are necessary to ensure a successful intervention. This will include some long-term plans to prevent future outbreaks, if this is practical.

The final step in handling a disease outbreak is often the most neglected. Communicating the findings and the success (or failure) of the control measures implemented provides valuable information to other veterinarians facing similar outbreaks. Local or state veterinary association meetings, veterinary e-mail discussion groups, and veterinary journals are common forums for disseminating such information. It is also important to share your findings with your health

department and state public health veterinarian if the disease is zoonotic or the outbreak has other public health implications. Summarizing the findings for publication by local newspapers or in community newsletters may also help educate owners about preventing the illness in their pets. Omitting this final step may result in repeated efforts by other veterinarians to solve the same problem with varying degrees of success, to the detriment of the animals in the population at risk.

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12

Preventing Disease and Promoting Health in Veterinary Patient Populations

Much of clinical practice has traditionally been focused on treating ill or injured animals. In recent decades, food animal practitioners have instead begun to emphasize prevention of disease and integrated health management programs. The ability to document the influence of these programs on the improvement of farm income and reduction of costs has provided leverage for veterinarians to change farmers' or managers' views about the need for routine preventive programs.

In the 1980s and 1990s, veterinarians in companion animal practice (e.g., dogs, cats, some horses, or pocket pets) also began to recognize the importance of preventing disease. With a growing emphasis on the human-animal bond, active promotion of health rather than just prevention of disease has begun to be embraced and discussed. Health promotion in the form of a proactive stance on behavioral problems, nutrition counseling, and even appropriate pet selection have begun to be integrated into the practice setting. Many different terms including herd health and productivity, preventive medicine, health promotion, and population medicine have been used and defined. For the purposes of this book, population health programs (PHP) are used to indicate a set of activities designed to prevent or control diseases in groups of animals.

Disease prevention may be more economical, more efficient, and more desirable in both food animal production and companion animal settings. The advantages in farm settings are well documented and promoted, even though veterinarians in private practice have tended to be slow to emphasize preventive programs over "fire-engine" medicine. In companion animal practice, where the emphasis is often on the individual patient, preventive programs have been implemented in an intermittent and selective way, most notably with services like vaccinations and fecal examination for parasites. Population-level health issues are commonly seen in companion animal

practice in the form of barns of horses, breeding catteries, animal shelters, boarding kennels, and multiple pet households. In settings such as boarding facilities or animal shelters, economics influence the role and scope of disease prevention for companion animal practitioners, making the development of programs to optimize animal health and disease prevention an ongoing need. Although there are limited scientific data available on the economical impact and efficiency of integrated health promotion and disease prevention programs in companion animals, with the emotional considerations of lengthy or painful illness, prevention of disease is clearly warranted.

General Goals in the Creation of Population Health Programs

The basic goals and approaches for PHPs are similar for all species. The goals are (1) identify the problems of interest for the species and management system (Table 12-1); (2) determine the relative importance of the problems, including animal welfare and economic concerns; and (3) develop methods to track, improve, and monitor the problems. Implementing these goals requires information from the client (e.g., farmer, producer, manager, or owner) about events, management practices and performance, any additional external performance information (e.g., DHIA records, inspection information at slaughter, euthanasia rate in a shelter, number of healthy puppies

Table 12-1. Considerations in Selecting Problem(s) of Interest in a Disease Prevention Program

Importance of Problem of Interest	Example Problem
Economic	Milk production in dairy cattle Competitive edge in a 3-day event horse Kennel cough in a boarding facility
Humane	Euthanasia due to feline upper respiratory disease in an animal shelter Lameness in a flock of sheep Strangles in backyard horses
Zoonotic	Ringworm in a cattery Salmonella in chickens Scabies in a multiple dog household

produced), and veterinary findings including physical examination, laboratory results, and necropsy. These data allow for analyses that provide immediate warning of a problem in the short-term, as well as long-term, comparison with other similar facilities and data to implement and evaluate performance or health objectives.

The goals may be developed and implemented at the level of a farm, barn, or specific housing unit; the veterinary practice; or the individual household. At the level of the dog or cat practice, the program would be implemented for each patient and client in the form of practice guidelines or wellness programs. For multiple animal households and practice level programs, visits to

the premises are unlikely except for house call practices. For most other situations, visits to the facility or farm may be required to acquire enough information and provide the needed services to the animals.

The importance of the veterinarian-client-patient relationship in this context cannot be overstated. The owner or manager (client) must be willing to work with the veterinarian and agree on goals, keep needed records, follow health protocols, and implement changes (Box 12-1). The role of the veterinarian in developing and maintaining a program is complex (Box 12-2). Programs that are practical to implement within the existing system, provide meaningful feedback to the client, and include all the important stakeholders are most likely to succeed.

Box 12-1. Some Considerations for the Owner or Manager Embarking on a Successful Disease Prevention Program

1. The ability to communicate and cooperate with the veterinarian, other staff and experts.
2. Records on individual animals or units of animals (such as flocks of poultry).
3. Participation in available educational programs.
4. Enough business sense to make decisions that will work in the long term.
5. Clear idea of the goals of the particular animal "herd" or group.
6. The authority to implement and enforce the program.

Box 12-2. Role of the veterinarian in population health programs

1. Stimulate the owner/manager to consider a comprehensive program.
2. Provide diagnosis and treatment of the illness or illnesses.
3. Provide emergency care if required.
4. Provide medications and vaccines.
5. Advise on nutrition, housing, behavior, hygiene, and animal welfare.
6. Advise on production techniques for the species involved.
7. Provide access to experts in necessary areas including public health and government agencies.
8. Provide feedback to the owner or manager on health and economic issues.
9. Provide expertise in clinical epidemiology include testing, data collection and decision analysis.
10. Provide regularly scheduled visits and calls to the premises.

Using Clinical Practice Guidelines in Veterinary Practice

Because most of the existing practice guidelines pertain to PHP, information on evaluating them is included in this section. Veterinarians have historically been a very independent group when it comes to putting guidelines or protocols in place, in spite of an increasing movement toward accountability, high standards of care, and an emphasis on client education. However, with the advent

of multiperson practices, corporate practice, and the knowledge explosion, some guidelines have been developed for private veterinary practice. If well designed, these guidelines can provide a fast summary of large quantities of information on a pertinent topic. Guidelines are often developed using a diversity of approaches, but Box 12-3 provides some ideas that are important considerations before implementing guidelines. The more "yes" answers, the better and more trustworthy the guidelines.

Clinical practice guidelines in veterinary medicine that are widely cited include vaccination protocols for dogs and cats, and recommendations for handling suspected injection-associated sarcomas in cats as examples. For dogs, vaccination guidelines are on the internet at www.ivis.org. This web site is designed to be an

Box 12-3. Key elements for clinical practice guidelines

1. Was the information collected in an organized, well-described fashion?
2. Was the information evaluated with regard to the quality of the studies or data included?
3. Was factual information clearly separated from opinion?
4. Were the guidelines peer reviewed?
5. Were the authors or organization reputable?
6. Were the benefits and costs of implementing the guidelines clearly presented?
7. Are they likely to be current and incorporate new information?

expanding and updated textbook, written by recognized authorities in the field. These guidelines do not specify the sources or methods by which data were collected. Peer review is performed in a limited way, but the articles on the web site primarily represent the work of the authors. For cats, the American Association of Feline Practitioners has published the vaccination and sarcoma guidelines (among other feline practice guidelines) on their web site www.aafponline.org. The vaccination guidelines were developed by two expert panels and have been endorsed by several other organizations. Again, the source and method of information collection is not made explicit. Guidelines for sarcomas are periodically distributed through a variety of printed formats as well.

General Approach to Population Health Programs

In general, these programs have four components (1) reproduction, (2) disease control and prevention, (3) nutrition, and (4) production and performance. Animal welfare and protection of the environment are usually subsumed within these four areas.

Reproductive concerns may take the form of increasing reproductive efficiency (number of services), eliminating reproduction (spaying female dogs), or optimizing reproduction in some fashion (increasing

the frequency of twin lambs). The specifics depend on the species, use, management scheme, and many other factors.

Disease control (reducing the morbidity and mortality from the disease) and prevention can take many forms. See Box 12-4 for general areas to consider in understanding and designing control and prevention programs. There are also commonly strategies for controlling or preventing disease (Box 12-5), which need to be tailored to the situation, with particular emphasis on the economic issues involved.

Nutrition deserves a brief discussion because it has sufficiently far-reaching and widespread effects for all species. It is critical in food animal settings for its effect on reproduction, weight gain and carcass quality, disease resistance, and economic trade-offs. In companion animal settings, nutrition also plays a role in disease resistance and the immune system, cost concerns, and performance (reproductive and athletic). But because of the special relationship that sometimes exists between companion animals and their owners, pet food and pet food marketing have become a huge business. The food fed an animal is not necessarily chosen for its optimal nutritional content but because the cat likes it; the owner prefers the convenience, smell, or appearance; or because of successful advertising. Furthermore, feeding a beloved pet is often an emotionally charged process not a rational one. Because of this, obesity likely affects more than

Box 12-4. Factors to Consider in Preventing and Controlling Disease

Animal Related
Species
Age
Maternal immunity
Concurrent disease
Disease resistance and genetics
Reproductive status
Nutrition
Stress level
Health history

Agent Related
Specific pathogen or exposure
Existence of effective diagnosis and treatment
Control of vectors and other modes of spread
Dose and route of infection
Zoonotic implications
Severity of clinical disease

Environment Related
Type of housing
Population density
Sanitation
Weather, temperature, and humidity
Social interactions

Time Related
Time of year
Time of day
Recurrent pattern
Recent changes or introduction of new

Box 12-5. Strategies for controlling or preventing disease

1. Scheduling of routine physical examinations.
2. Controlling internal and external parasites.
3. Appropriate use of vaccinations and preventive care (such as foot trimming).
4. Carefully considered protocols for introducing new animals (including isolation, testing for disease).
5. Specific approaches for handling animals with clinical illness.
6. Evaluation of housing and nutrition for their effect on animal stress, disease spread, and behavior.
7. Hygiene and use of general cleanliness, as well as appropriate disinfection agents.
8. Legalities regarding reportable diseases, zoonoses.
9. Using the records to track targeted diseases and efficacy of interventions as well as look for new problems.
10. Balancing cost, welfare, production, and client desires in the design of the program.

30% of dog and cat patients in practice (and possibly a substantial number of backyard equine patients as well).

Performance and production span the full spectrum from purely economic food production to athletic competition to animals with specific jobs as assistants to people to being good companions. Organizations for each species or activity are potential sources of specific, useful information for performance or production. Veterinary specialists in extension, practice, or veterinary schools are also good resources.

Face-to-face interactions between the veterinarian, the client, and patient or patients will be necessary to implement disease prevention programs successfully. In most farm situations, the veterinarian will go to the patient. This will also be true for some of the companion animal situations because first-hand observation of the housing and management as well as the animal will be necessary. Regardless, there should be a regularly scheduled visit, either at the time important events occur (lambing season) or on a regular (monthly or semiannual) basis, depending on the management scheme and specific situation.

Record keeping is critical for the design, implementation and success of the program. If any records are already being kept, these can be used as the basis for identifying the problems and prioritizing them. In food animal settings, this is not as big a problem as in companion animal settings, but the records may still be difficult to locate and examine if they are not computerized or the farm owner or manager is not diligent about recording health and treatment information.

Guidelines for Disease Prevention or Health Promotion Programs in Practice

In general, programs of this sort for food animals are presented in the veterinary curriculum and in the major

text books. Some suggested general and species specific references are listed at the end of the chapter.

In some states, the state agricultural services may have helpful information. In Florida, the Department of Agriculture and Consumer Services in partnership with University of Florida has developed a voluntary certification program for food animal producers. It is based on a firm understanding of herd health issues (environmental health, control of disease and food safety issues regarding medication administration) and is designed for medium to small producers.

Although the overall structure and points to consider in designing a PHP are shared in nearly all settings, obviously the details must be tailored to the specific population and location. These details (such as specific vaccines and intervals, wormers, disinfectants) should be incorporated into the PHP based on their proven worth using the guidelines for evidence-based care whenever possible. Modifications based on the location (region, country, climate) will need to be made to address diseases and management issues that are important influences on health.

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13

Companion Animal Population Health Programs

The majority of graduating veterinarians are going into companion animal practice. Therefore, this chapter focuses on dogs, cats, and horses in the practice setting because little information about PHPs in these species has been published in readily accessible locations. In most private practice settings, there are often components of disease prevention programs (such as heartworm screening and prevention in dogs), but comprehensive PHPs have been rarely implemented. The controversies of the late 1990s and early 2000s over vaccination

frequency and type in dogs and particularly cats highlights one component of what are commonly referred to as “wellness” or “life-cycle” programs. Historically the annual visit with physical exam and required vaccinations was the cornerstone of dog and cat practice. With the development of recommendations to tailor vaccination programs to the animal’s specific level of risk, the focus of the annual visit must and should change. Practice guidelines for vaccinations of cats (www.aafponline.org) and dogs (www.ivis.org) are available on the web.

Population Health Programs at the Level of the Veterinary Practice

The components to consider in a wellness program for pet dogs and cats at the practice are similar, although a variety of approaches are possible. The guidelines included here (Box 13-1) use the approach of Catanzaro, in which the annual examination is a life-cycle consultation with the veterinarian that qualifies the pet and owner for “preferred client” status for the following year. This status then provides for shorter visits that heavily involve the technical staff, although the client may opt for a consultation with the veterinarian. Pricing, services, and continuing education of the staff will all need to be tailored to the practice. This approach emphasizes the importance of the pet and the continu-

Box 13-1. Components of a Population Health Program for Pet Dogs and Cats in Veterinary Practice

1. Vaccinations adapted to the exposure and immune status of the pet. This should include a critical evaluation of new vaccination products.
2. Identification, control, and routine prevention of external parasites (fleas, ticks, mites).
3. Identification, control and routine prevention of internal parasites (intestinal parasites and heartworm—consider prevention in cats).
4. Spaying or neutering of dogs and cats.
5. Nutritional advice, especially in the prevention of obesity.
6. Grooming advice or services.
7. Behavior advice (concerning normal and expected behaviors, pet selection, basic training) and/or referral (for training or behavioral problems).
8. Dental examination, cleaning, and polishing.
9. Routine screening or testing programs (many have been suggested, few have been evaluated to determine if early disease detection provides better outcomes or reduces morbidity or cost). Heartworm disease in dogs and feline leukemia and feline immunodeficiency viruses in cats are currently the most appropriate in general practice settings.
10. Special lifestyle risks (e.g., pets that travel, hike, are located in an area with endemic disease).
11. Other client education materials in the form of brochures, newsletters, and videotapes.

ing connection between the client and the practice for all needed assistance. The selection of specific vaccines, target parasites, and screening tests must be made based on the best available information and be adjusted for the specific location.

There are special considerations for multiple pet households, breeding or boarding kennels, and animal shelters (both limited admission, longer holding period and open admission, high-turnover facilities). In these settings, the health and performance of the group of animals may be as or more important than the health of individual animals. This is a genuine shift from the usual clinical situation in small animal practice. Economics tends to play a more important role in these settings as well, either because of the numbers of animals involved or the business aspects of the facility. Control of infectious and zoonotic diseases becomes much more important and difficult. Stress and behavioral problems and the impact of these on health also become increasingly pressing issues. And in breeding kennels, reproductive performance beyond spaying and neutering will become prominent components of the program.

Multiple pet households (three or more of one species) fall somewhere in between breeding kennels and animal shelters in the types of problems encountered, depending on the situation. For relatively closed populations, management of chronic health problems

and behavioral issues assume a prominent role. For households with animals coming and going through adoption, rescue, fostering or competition, control and prevention of infectious diseases is a greater concern. In some households where cost is a major factor, marginal or subclinical nutritional deficiencies may be present due to purchasing the cheapest food available. Households with mixtures of dogs and cats may have more problems with parasites, such as fleas, that are common to both.

Boarding facilities are businesses that house animals for relatively short periods (days to weeks) for a fee. Various other services (e.g., grooming, walking, playing, training) may also be offered. These facilities have a more of a problem with infectious disease and nutrition because of the high turnover rate, stress of animals away from home, and possible changes in diet, feeding routines, and exercise levels. Most boarding operations have requirements for specific vaccinations before entering the facility. Remember the lag time between vaccination and protection by vaccines and the variability in duration of immunity when planning vaccination requirements for these facilities. As for multiple animal households, the guidelines have elements of both the breeding kennel and the animal shelter. There may also be local or regional requirements for licensing or inspection for these businesses.

Breeding Kennels and Catteries

Individuals who own or manage dog and cat breeding operations are varied in their purpose, expertise, and frequency of breeding. Breeders are usually self-identified, but the more reputable ones are involved with national or regional clubs, activities, or shows and have the improvement of the breed as a focus. They may also subscribe to a code of ethics promulgated by their breed club. Sources of information in addition to the references cited in this section are web sites from the national and regional breed clubs. Cat Fanciers Association, for example, has current articles on specific health problems written for breeders as well as general feline health information. The previously mentioned AAFP web site also has useful information.

Some markers of success in breeding facilities are number of kittens or puppies weaned, level of morbidity and mortality in the neonatal and weaning periods, breed champions with demand for offspring, animals with the desired good temperaments and health. For dogs, success in various sports such as agility, obedience, field trials, hunting, lure coursing, or herding may also be important. In general, the larger the population, the smaller the role of treatment and the larger the role of prevention. The facilities have a major impact on ability to provide good management and medical care. For small operations, the animals are part of the family and

are kept much like any pet. This can cause some difficulties in terms of disease control and population density. Management of the kennel or cattery is designed to create a healthy environment with low stress, protection from the weather, good reproduction, and healthy puppies and kittens. See Box 13-2 for guidelines to develop PHP in breeding operations.

Animal Shelters

For animal shelters, good resources for specific health issues include the Humane Society of the United States (www.hsus.org/programs/companion/shelter_library), the American Humane Association (www.americanhumane.org; publications available), ASPCA (www.aspca.org), and regional animal control or humane society organizations. A program beginning in 2001 at the University of California, Davis, is the Maddie's Shelter Medicine Program (www.vetmed.ucdavis.edu/ccah/prog-sheltermed/sheltermedicine.htm), which should offer shelter-specific PHP. HSUS has seven recommended policies for every animal shelter. Several are controversial in some circles (especially the first two) or impractical for certain settings, but they form a useful orientation for veterinarians unfamiliar with the general operation of well-organized animal shelters (www.hsus.org/programs/companion/shelter_library/seven_policies.html). These policies are the following:

Box 13-2. Components of a Population Health Program for Breeding Kennels and Catteries

1. Regular observation of animals for problems.
2. Record keeping with individual animal identification (tattoo or microchip) and health information to include age, sex, number, and location of animals.
3. Routine preventive visits.
4. Laboratory diagnosis of disease (for correct prevention and treatment); necropsy of all animals, including stillborns.
5. Nutrition specific to life stage and use or activity of animal.
6. Vaccination in conjunction with sanitation, ventilation, and housing protocols.
7. Parasite control in conjunction with sanitation and housing protocols.
8. Breeding protocols for detecting and preventing problems (e.g., *Brucella canis,* infertility, heat detection, mastitis, metritis, eclampsia).
9. Neonatal and weaning protocols for detecting and preventing problems (infectious, behavior and genetic).
10. Stress detection and intervention (indicated by high prevalence of chronic respiratory or gastrointestinal disease or behavioral changes).
11. Selecting or culling of breeding animals due to performance or medical problems; for catteries, test and removal for feline leukemia virus (FeLV) or feline immunodeficiency virus (FIV) is recommended.
12. Quarantine for incoming animals 3 to 6 weeks, with testing for infectious diseases, vaccinations, fecal examination, treatment for parasites, fungal culture (cats).
13. Evaluation of outgoing animals (e.g., physical exam,

temperature, appetite, and feces).
14. Adequate and healthy social interactions with other animals and people.
15. Housing, ideally with separate areas to avoid mixing of different age groups and to allow handling of animals from most to least susceptible. This would include at least areas for whelping, other healthy animals, quarantine, and isolation (for ill animals).
16. Cage/run size (for government regulatory requirements: www.nap.edu/readingroom/books/labrats/; www.aphis.usda.gov/ac/publications.html.
17. Assessment of population density.
18. Sanitation of all areas, especially where urination, defecation, sleeping, and feeding occur.
19. Ventilation and air turnover. In general, if odor is a problem or the humidity is higher than 70%, ventilation is inadequate.

- Accept all animals brought in (open admission shelter compared with limited admission, no-kill shelters)
- Do not charge for individuals to bring an animal in, their own or a stray
- Provide a clean, safe, healthy environment for the animals (including at least a rudimentary PHP)
- Hold stray animals (those not brought in by their owners) for at least 5 days including a Saturday
- Screen adopters using specific guidelines
- Use sodium pentobarbital as an injectable euthanasia product, administered by trained personnel

- Spay or neuter all animals before adoption or guarantee that all are sterilized after adoption (and before breeding)

For shelters, control of infectious and zoonotic diseases are often the primary problem, and modification of the usual veterinary practice protocols for vaccination, worming, and disinfection is needed. In general, the population of animals at a typical shelter is heterogeneous in terms of age, health history, current health status, and level of socialization. The type of shelter (e.g., cat only, limited admission with long-term holding, open admission with short-term holding, animals from owner surrender, and animals from animal care and control agency) determines some of the specific details of the program. Similar to breeding kennels and catteries, the actual facility has a substantial impact on the types of problems encountered and the options for control. A comprehensive and effective PHP is important not only for the welfare of the animals but also for the reputation of that shelter in the community and for employee moral and shelters in general. See Box 13-3 for guidelines on PHP in shelters.

Horse Population Health Programs

Horses are the species that most commonly have issues unique to both animals as companions and animals with economic and performance issues. In general, Box 13-4

Box 13-3. Components of a Population Health Program for Cats and Dogs in Animal Shelters

1. Evaluation of incoming animals to include stress level, health, and socialization. Decision about adoptability made as early in the process as possible.
2. Incoming animal quarantine (if possible, 5 to 8 days). Test, deworm and vaccinate at entry.
3. Record keeping including health data.
4. Written protocols and staff training with periodic reevaluation.
5. Program monitoring for successful disease management and adoption.
6. Adoption criteria based on medical and behavioral criteria.
7. Methods for appropriate manual and chemical restraint.
8. Internal and external parasite identification, treatment, and control protocols.
9. Vaccination protocols modified for ages and common problems in the shelter (for example, intranasal vaccines pros and cons, and use of modified live measles vaccine in young puppies).
10. Sterilization procedures (in house or with local veterinarians, before leaving the facility or by contracts, before adopted or after new owner has indicated interest in adoption, use of prepubertal spay or neuter).
11. Control of stress levels (to decrease infectious and behavioral problems).
12. Zoonosis identification and control.
13. Nutrition to address different life stages, feeding and storage protocols, use of special diets, and fecal output.

Continued

Box 13-3. Components of a Population Health Program for Cats and Dogs in Animal Shelters—cont'd

14. Housing (for optimal disease control and stress management), including separate areas for incoming, obviously ill animals (isolation and staff handling protocols), and animals to be euthanized or to be adopted.
15. Sanitation to include physical cleaning and chemical cleaning (safety and efficacy [for example, phenol toxicity in cats]) .
16. Ventilation: 10 to 12 air changes per hour is a suggested starting point; intake and exhaust locations to prevent recirculation of contaminated air
17. Traffic flow in shelter from least to most contaminate d areas.
18. Legislative concerns such as reporting of bites and specific diseases, as well as other injuries.
19. Local education about shelters and pet population issues.
20. Euthanasia program, including criteria for euthanasia, appropriate restraint and methods for performing euthanasia, staff training, and dealing with staff stress.

lists common components of a PHP for horses, with emphasis on horses as companions.

Horses that are used for breeding, working, or performing in athletic events require unique modifications of the general PHP. The economics, owner attachment, and use of the horse determine the particular modifications that are necessary, particularly in regard to husbandry, nutrition, vaccination, and deworming.

Box 13-4. Components of a Population Health Program for Companion Horses

1. Deworming program appropriate to the husbandry, numbers, age, and use of the horses.
2. Regular foot trimming with or without shoeing.
3. Dental check every 1 to 2 years depending on age and history.
4. Administration of appropriate vaccinations including rabies.
5. Advice on cleaning stalls, paddocks, runs, and disposing of manure.
6. Advice on pasture management, including clipping and rotation.
7. Nutritional advice including prevention of obesity.
8. Description and integration of exercise and turnout program.
9. Behavioral advice (normal and expected behaviors, referral if needed).
10. Presence or type of insurance.
11. Advice and oversight of record keeping.
12. Information on horse travel regulations, introducing new horses, prepurchase examinations.
13. Client education materials in the form of brochures, newsletters, and videotapes.

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14

Basic Statistical Concepts

Data are the pieces of information that are collected or recorded for the variables or characteristics of interest. In general, all studies, projects, and investigations should include a section on **descriptive data**. These data include the pertinent background or demographic information, a summary of the results from variables studied, and any other potentially important figures. The background or **demographic information** provides a picture of the population of animals involved and may include their age, breed, sex, species, reproductive status, production status, function, coat color, and health status.

Types of Data

The type of data or variable is important because it determines the type of summary measurement and statistical analysis that can be used. There are two main types of data: continuous and categorical. **Continuous data** can take on a spectrum or continuum of values within a range (which may be infinite). Continuous data (sometimes called quantitative or interval data) may be further subdivided (using a variety of terms) but for most purposes, if the data are continuous, they are handled similarly with regard to summaries and statistics. Examples of continuous data are weight, age, body temperature and blood glucose.

Categorical variables measure characteristics which are divided into classes or subgroups. There are two main types of categorical data: nominal and ordinal. **Nominal variables** have subgroups that have no numeric relationship to one another such as breed or coat color. There is no ordered or numeric relationship between being a Jersey, a Hereford, or a Brahma cow. The breeds are just names assigned to the different subgroups. **Ordinal data** consist of classes or subgroups that have some sort of ranking system or inherent order to them such as lameness scores (1 to 5), severity of heart murmurs (grade 1 to 6) and severity of cellular infiltrates (mild, moderate, severe). There is a clearly ordered relationship between the classes but there is not a pre-

dictable numerical one. So, a grade 2 lameness is not as severe as a grade 4 lameness. A special type of categorical variable has only two categories and is called a **dichotomous** variable.

Summarizing Data

The goal of summarizing data is to provide a quick picture of the many individual animals' information. Continuous variables are summarized using means, medians, or modes. These measures provide an indication of where most of the individual observations tend to occur. The **mean** is used for normally distributed data. Data that are normally distributed fall on a bell-shaped curve if plotted out, the mean is close to the median, and the mean and median are half way between the largest and smallest value. The mean is the sum of all observations divided by the number of observations and is often referred to as the average. The **median** is used for data that are skewed, where there are individual observations that are far away from the others. The median is the middle value counting from the highest or lowest observation. The **mode** would be used for continuous data that tended to have more than one peak if plotted graphically. It is defined as the most common value in the data set and is rarely used in the clinical literature.

Another component of summarizing data is to provide some estimate of variability. This variability may be

considered to be the "noise" or spread of the observations around the mean or median. For the mean, the **standard deviation** or **variance** is used. The variance is the square of the standard deviation. The standard deviation has the property that the mean plus and minus two standard deviations include 95% of all the observations if the data are normally distributed. For the median, a range or percentile is used. The **range** is the highest and lowest value observed. A **percentile** indicates what proportion of the observations fall above or below that value. So the 75th percentile is the point at which 25% of the observations have a higher value and 75% a lower one. The median is the 50th percentile because half the observations fall above and half below. Ranges and percentiles can be used with means as well.

In many cases, a picture is still worth a thousand words. Graphic displays commonly include histograms, box and whisker plots, dot plots, and scatter plots. These provide a visual summary of the individual data and may include information about the numeric summary as well.

One other concept is needed to understand the choice of statistical tests (and sometimes study design). This is the idea of independent data as compared with paired or related data. **Independent** observations have no inherent reason to be similar or related to one another. **Paired** data come from repeated measurements from the same animal, measurements from litter-

mates or animals that are matched on some important characteristic like age or sex. Data obtained from the same animal across time would be expected to be more similar than data obtained from different animals. For example, blood pressure measured at 1-hour intervals five times on the same animal (paired or blocked data) would be more similar (have less variability) than blood pressure measurements on five different animals (independent data).

Comparing Data

Comparing data can be done by visual inspection (the "eyeball" test) or by more formal statistical analysis. Increasingly, statistical analysis is used and published, in part because of the ease of performing tests in many of the menu-driven statistical packages. Most statistical tests answer the question "is there a difference between the groups?" The difficult part is that the study data being analyzed are usually a sample (horses seen at a teaching hospital with colic) or subpopulation of the animals that are of true interest (e.g., all horses seen by all veterinarians with colic). There are two main problems because we are using a sample of the true population of interest (called statistical inference): (1) the population studied may not be representative of the true population and (2) the statistical test may not provide the correct answer. The first problem is usually an

issue of appropriate study design, and the veterinarian must make an decision based on subject matter knowledge as to whether the sample population is appropriate.

The second problem relates to the nature of statistical inference. The statistical test provides a measure of how likely it is for the differences between the groups to be due to chance alone if there is not a real difference between the groups. This measure is the ***P* value**. In statistical analysis, the *P* value can range from nearly zero to nearly one, but tradition has decreed that a *P* value of 0.05 is the cut-off point for deciding whether or not there is a difference between the groups. If the *P* value is less than 0.05, then the groups are declared different (a **statistically significant difference** is found), if greater or equal to 0.05, then the groups are not different. The problem is that a *P* value of 0.05 means that 5% of the time the results found could still be due to chance alone and not due to a real different between groups. Therefore, using a *P* value (or **significance level**, the cut-off point at which statistical significance is declared) of 0.05 means that 5% of the time, the investigators will declare a difference between the groups when one really does not exist. This is analogous to the false-positive rate in diagnostic testing and is called a **type I** or alpha error in the context of statistical testing. Sometimes, the investigator declares that there is no difference between the groups where there really is one (often due to a small

number of animals in the study). This is called a **type II error** or beta error and is analogous to a false-negative finding in diagnostic tests. If the type II error rate is subtracted from 1, a quantity called the **power** is found. The power is the ability of the study to detect a difference between the groups when there really is a difference between the groups.

It is crucial to realize that it is possible to have a statistically significant difference without a clinically important one, and vise versa. With a large number of animals, a drop in blood pressure of 5 mm Hg using indirect measurement could be found to be statistically significant. Yet from a clinical perspective, a medication that lowered pressure an average of only 5 mm Hg would not be very important, especially given the inherent difficulty in accurately measuring blood pressure in the first place. Table 14-1 summarizes some of the common statistical tests and how they could be used based on the type of variable, number of groups, and independence of the data.

Sometimes the objective is not only to compare but also to predict the likelihood (or probability) of an outcome given a set of measurements (Table 14-2). For example, a study could evaluate diet and lifestyle as possible predictors of survival in hyperthyroid cats. From a list of many different dietary and lifestyle variables, a small number that are significantly associated with survival could be determined. Because the outcome is time to death, survival analysis would be used. Alternatively, a

Table 14-1. Common Statistical Tests to Compare Data

Type of Data	Comparison For	Independent Data	Dependent Data
Categorical	Proportions or percentages	Chi-square	McNemar's chi-square
Normal continuous	2 means	T-test	Paired t-test
Normal continuous	> 2 means	Analysis of variance (ANOVA)	Repeated measures ANOVA
Normal continuous	Lines	Pearson's correlation coefficient	—
Skewed continuous, ordinal >4 categories	2 medians	Mann-Whitney/rank sum test	Wilcox in signed rank
Skewed continuous, ordinal >4 categories	>2 medians	Kruskal-Walis nonparametric ANOVA	Friedman nonparametric ANOVA
Skewed continuous, ordinal >4 categories	Lines	Spearman rank correlation coefficient	—

Table 14-2. Statistical Tests to Predict or Explain (Model) Relationships between Variables

Type of Outcome Variable	Common Statistical Test
Dichotomous (2 categories)	Logistic regression
Continuous	Linear regression
Time to an event	Survival analysis

study may be designed to explain how some variable is related to some other set of variables. For example, the objective could be to determine the relationship between age, breed, sex, and weight of the horse and the occurrence of laminitis (yes or no). This would be done using logistic regression because the outcome is a dichotomous variable (laminitis yes or no).

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Appendix 1

Qualitative Study Evaluation

Many types of studies use interviews and surveys. However, qualitative studies using interviews have a primary goal of examining people's beliefs and how these beliefs affect behavior or investigating complex cultural or societal attitudes. The interviews used are often relatively unstructured, and the number of participants are determined by reaching a point in the study where the ideas and perspectives that are expressed are no longer new. These studies also must be clearly thought out and conducted in an organized fashion. These studies are relatively rare in veterinary medicine, but they are increasing in frequency as the importance of the relationship between people and animals becomes incontrovertible and recognized as a factor in health-related decisions. Some guidelines for these qualitative studies are outlined in Box A-1. The results of qualitative studies are helpful if they apply to other clinical settings, resonate with other groups of people, and prove useful in understanding clients in similar situations.

Box A-1. Key Elements for Studies about Perceptions, Beliefs, and Attitudes

1. Is a qualitative approach the most appropriate one for the question?
2. Is there a clearly defined group of people included in the study who could address the question of interest?
3. Does the data collection method access the important information and consider all relevant factors (is it comprehensive)?
4. Are the data analyzed and summarized so that the evidence supports the conclusions?
5. Are there other checks and balances on the data analysis and other sources of information that make the results believable?

In the veterinary literature, owner perceptions are rarely addressed, and when they are, it is usually in a very structured, quantitative fashion. However, further exploration of the reasons behind this perception or the background that led to them would prove very useful in many veterinary settings. For example, a study in Michigan on equine health problems asked owners or barn operators to rank the top five health problems in the equine industry.[1] Three of the owners top five were not included in the top five diseases based on frequency, duration, lost of use of the horse, or fatality risk. The authors speculate that personal experience, disease

severity, and other factors may account for the discrepancy. A qualitative study addressing these reasons could provide useful information about health care choices and preventive programs for veterinarians working with horse owners.

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Appendix 2

Comparing Two Diagnostic Tests

Comparing Tests with One Another Without a Gold Standard

To evaluate formally agreement between tests that have categorical results when no gold standard is available, a statistic called kappa is commonly used. **Kappa** provides as estimate of agreement that takes into account agreement due to chance. Kappa is also used to evaluate the agreement between different doctors, technicians, and techniques. Observed or **simple agreement** is the sum of the observations that match. So if two radiologists were evaluating the same hip radiographs for dysplasia, a table such as Table A-2 might be generated.

One set of guidelines for interpreting kappa is: >0.81, excellent agreement; 0.61 to 0.81, substantial agreement; 0.41 to 0.60, moderate agreement; 0.21 to 0.40, fair agreement; 0 to 0.20, poor agreement. Another widely used guideline suggests 0.4, poor; 0.4 to 0.75, fair to good, more than 0.75, very good to excellent. Often the authors will indicate their guidelines for interpreting agreement.

Table A-2. Calculation of Agreement Using Kappa and Observed (Percent) Agreement

	Radiologist 2 Normal Hips	**Radiologist 2 Dysplastic Hips**
Radiologist 1 normal hip	14	4
Radiologist 1 dysplastic hip	3	13
	17	17

Observed agreement: 14 + 13/34 = 0.79
Chance agreement: (17 * 18)+ (17 * 16)/(34 ^ 2)= 0.5
Kappa = (0.79 – 0.5) / 1 – 0.5) = 0.58

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Appendix 3

Calculating Test Accuracy and Predictive Values: Another Look

Laying out a table to calculate predictive values using information in an article

1. Create the outline of a 2×2 table as in Table 6-1.
2. Select a total number of animals for the calculation. This number should be chosen for convenience such as 100 or 1000.
3. Identify the appropriate prevalence.
4. Multiply this total number (N) by the prevalence as a decimal to get the total D+ animals (a + c).
5. Subtract D+ from N to get D- (b + d).
6. Multiply the sensitivity (as a decimal) by D+ to get TP or a. Get FN by subtracting TP from D+ ([a + c]-a).
7. Similarly, multiply the specificity by D- to get TN (d). Be sure to put this answer in the bottom box. Get FP by subtracting the TN from D+ ([b + d]-d).
8. Calculate predictive values as usual.

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Page numbers followed by "t" indicate tables; page numbers followed by "b" indicate boxes.

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